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Original Communications

NOW AND THEN*

A Statistical Review of the Progress of Midwifery During the Last Twenty Years With Thoughts for the Future

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JOSEPH PRICE made himself famous for all time by his splendid work on inflammatory conditions in the pelvis and by being the first to coordinate gynecology and abdominal surgery. His outstanding career was prefaced when, at only 24 years of age, he was appointed to the charge of the Obstetrical Department of the Philadelphia Dispensary; ten years later, to demonstrate that his interest in obstetrics was still very much alive, he took charge of the Preston Retreat and, during his seven years of duty there, no death was recorded from sepsis, a most noteworthy and unique achievement for those days. His was the enviable record of being the first to try and put obstetrics on an aseptic basis.

I may therefore be excused tonight for choosing a purely obstetric subject for this oration, which honors his memory. My title is "Now and Then" and records the progress of midwifery during the last twenty years.

There have been great advances in medicine and surgery during the last twenty years, but has midwifery also progressed? I propose to answer this question in the affirmative, and it is my endeavor to state what I take to be the main reasons for such success and even to suggest how further improvement might be achieved. In order to substantiate this claim, I have delved into the hospital reports for the past twenty years of five of the largest maternity hospitals in the British Isles and of the New York Lying-In Hospital. It is the result of these investigations that I intend to present. The first hospital which I have selected is the old Edinburgh Royal Maternity and Simpson Memorial Hospital and the new Simpson Maternity Pavilion of the Royal Infirmary, Edinburgh, to which the patients were transferred in March, 1939, because I have been a member of the Honorary Staff during these twenty years. (These hospitals are referred to as "The Simpson" in the Tables and Charts.) They com-

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memorate the name of Sir J. Y. Simpson, the centenary of whose discovery of the anesthetic and analgesic properties of chloroform is to be celebrated in November of this year. Simpson himself worked at the old Edinburgh Lying-in Hospital, which preceded the Simpson, so many of his case records are still in existence in the Hospital files. The other British hospitals are the Glasgow Royal Maternity Hospital and St. Mary's Hospital, Manchester, together with the Rotunda and the Coombe Hospitals in Dublin.

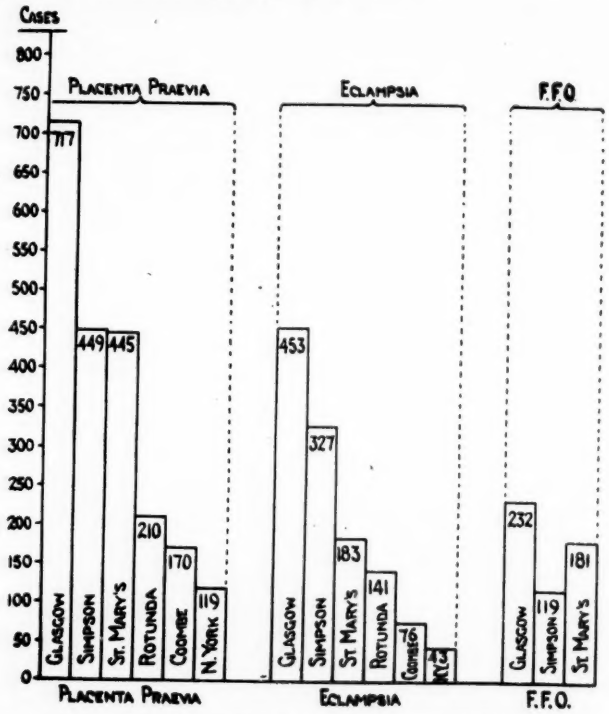

Fig. 1.—Comparison of hospitals with regard to some abnormalities during the last ten years.

In Great Britain and Ireland the large maternity hospitals all admit a varying number of antenatal and intrapartum emergency cases from general practitioners. These cases are termed "non-booked" cases, and are often admitted in anything but good condition, especially if admitted when in labor. These hospitals serve large areas and their emergency admissions vary as to numbers and severity; for instance, in the Glasgow Hospital, 55 to 60 per cent are emergency cases; at St. Mary's, 55 per cent; at the Simpson, 25 per cent; and at the Rotunda and the Coombe, 20 per cent. An indication of the numbers and the types of these conditions during the past ten years is shown in Fig. 1.

Placenta previa—

Glasgow, 717; Simpson, 449; St. Mary's, 445; Rotunda, 210; Coombe, 170; New York, 119.

Eclampsia—

Glasgow, 453; Simpson, 327; St. Mary's 183; Rotunda, 141; Coombe, 76; New York, 43.

Failed forceps outside—

Glasgow, 232; St. Mary's, 181; Simpson, 119; Rotunda, Coombe, and New York, not mentioned.

The Glasgow area embraces a population of well over two million and is in parts very poor and even squalid; rickets is still rife, though diminishing, and many of the emergency cases do not yet avail themselves of the antenatal supervision provided. St. Mary's Hospital, Manchester, also serves a large industrial population, but there are other smaller hospitals in the district which help to relieve it, and the population appears to have a better appreciation of the value of antenatal care. Though the Simpson Hospital, Edinburgh, admits practically all the emergency cases from the South East of Scotland, there is not the same poverty in this area, and practically all the emergency cases have had at least some antenatal supervision, maybe at times inadequate, by their general practitioners. The Dublin hospitals under review are two of three large maternity

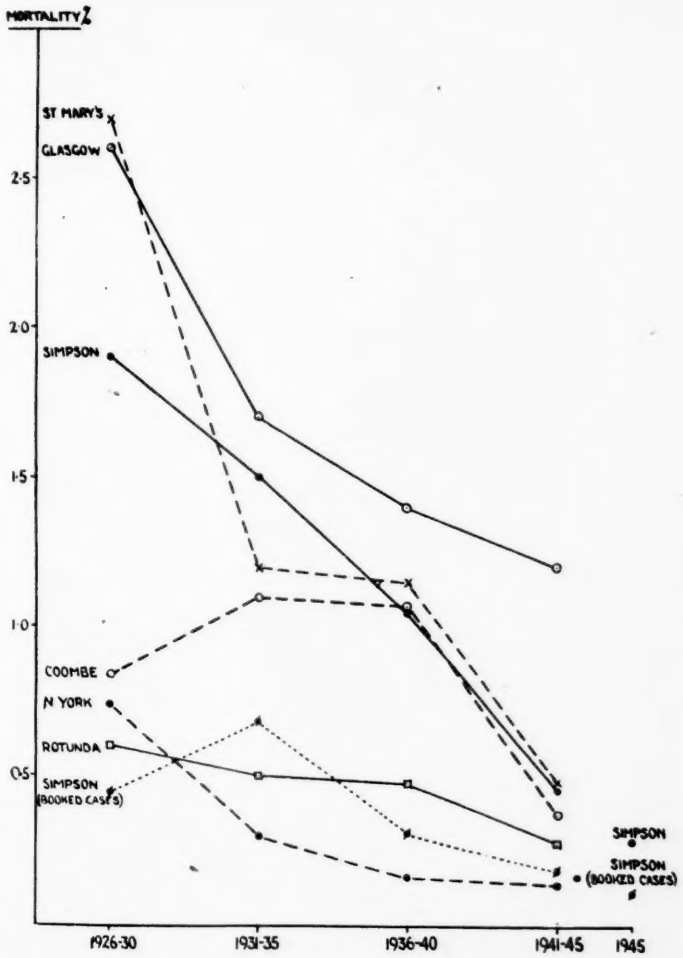

Fig. 2.—Mortality rates for six hospitals for four five-year periods.

institutions which serve the Dublin area, and therefore the emergency cases are divided. It is the admission of these "non-booked" cases which raises the maternal mortality and morbidity rates to compare unfavorably with hospitals which admit only cases supervised antenatally by their own staff. This important fact is also exemplified by contrasting the greatly decreased mortality and

morbidity in the "booked" cases (i.e. those who have attended the hospital antenatal clinics before admission) with the total mortality and morbidity of the hospital or with that of the "non-booked" cases. Again, a large number of the "booked" cases at all the hospitals are abnormal, being referred early to the hospital antenatal clinic, because of suspected dystocia or a bad obstetric or medical history; in Glasgow over 70 per cent of the total admissions are abnormal. The great decrease in the "booked" mortality figures as compared with the "non-booked" is very clearly seen in the mortality graphs of the last twenty years from the Simpson. (You will notice also that for the year 1945 alone the mortality rate is 0.28 per cent for all cases but is only 0.12 per cent for the "booked" cases, a point I wish to refer to again later.)

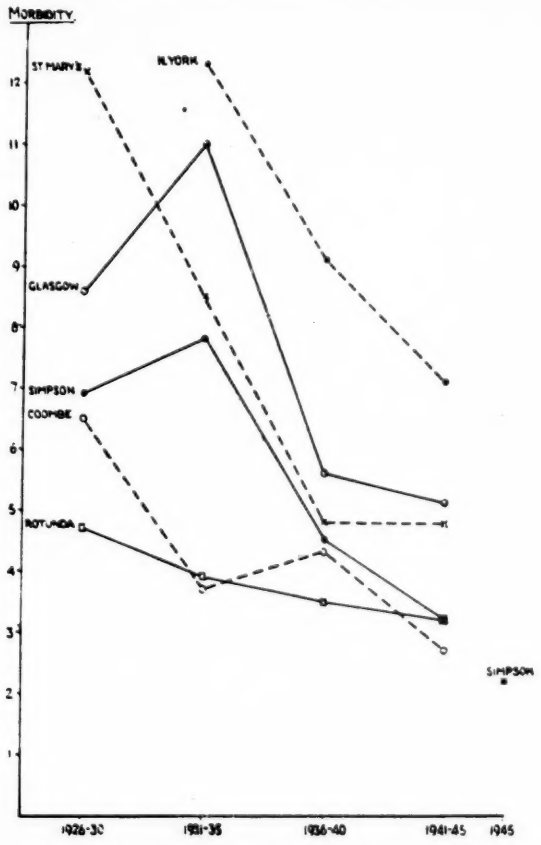

Fig. 3.—Morbidity rates for six hospitals.

The efficiency and obstetric reputation of a maternity hospital are primarily judged by its maternal mortality and morbidity and by its stillbirth and neonatal death rates. If, therefore, these rates show a marked decrease in the past twenty years, then one can justifiably assume that midwifery has progressed. The graphs of these rates for the various hospitals for five-yearly periods, beginning in 1926 and ending in 1945, to which I would now draw your attention, would appear to give striking evidence as to the progress midwifery has made during these years; all these rates are definitely lowered in all the

hospitals and though the mortality statistics of the New York Lying-In Hospital would seem to put the British hospitals to shame, it would not appear to be so bad as it seems at first sight, in so far as, in the case of the New York hospital, most of these cases seem to come under the "booked" category, and the figures for the Simpson "booked" cases for 1945 approach those of New York quite closely.

Morbidity for the British and Irish hospitals has been gauged by the B.M.A. standard as "All fatal cases and all cases in which the temperature reaches 100 degrees F. in any two of the bidaily readings from the end of the first day to the end of the eighth day after delivery"; the morbidity standard for the Lying-In Hospital, New York, however, is more strict, as the temperature is taken four-hourly, which probably accounts for its higher rate. These graphs show how morbidity has decreased.

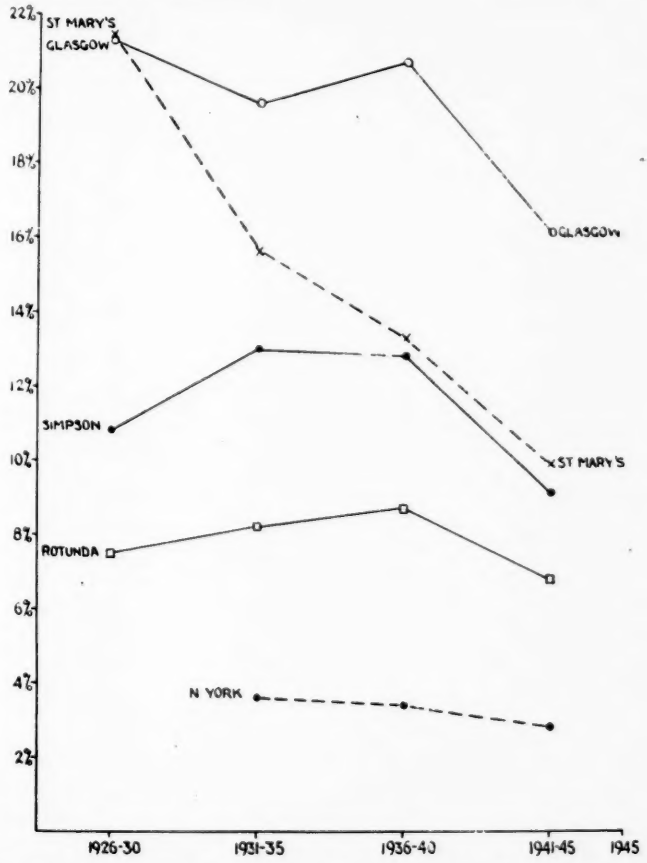

Fig. 4.—Stillbirths and neonatal deaths. Percentage of all cases at five hospitals.

Accepting that obstetric results have improved generally, I now propose to indicate in what direction this improvement has been achieved. I have tabulated the main causes of death in these hospitals for five-yearly periods, 1926 to 1930, 1931 to 1935, 1936 to 1940, and 1941 to 1945. These show, in the first place, how the hospitals compare with one another with regard to the causes of deaths, second, how the totals of deaths from the various causes have decreased

TABLE I. PRINCIPAL CAUSES OF DEATH (IN ORDER OF FREQUENCY)
The Simpson, Edinburgh

1926-30 Total Admissions—10,749			1931-35 11,652		1936-40 13,372			1941-45 18,640		
CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS
Eclampsia	50	0.46	Sepsis	38	0.33	Sepsis	26	0.19	Eclampsia	15	0.08
Sepsis	28	0.26	Cardiac	19	0.16	Eclampsia	15	0.11	Sepsis	14	0.07
Pre-eclampsia	14	0.13	Eclampsia	15	0.13	Pre-eclampsia	13	0.09	Cardiac	9	0.05
Rupture	14	0.13	Pre-eclampsia	15	0.13	P.P.H. and Shock	13	0.09	P.P.H. and Shock	8	0.05
Pl. Praevia	12	0.11	P.P.H. and Shock	11	0.09	Cardiac	11	0.08	Rupture	4	0.02
Hyperemesis	12	0.11	Pl. Praevia	11	0.09	Hyperemesis	9	0.07	Pl. Praevia	2	0.01
Cardiac	11	0.10	Hyperemesis	8	0.07	Pl. Praevia	8	0.06	Pre-eclampsia	2	0.01
P.P.H. and Shock	8	0.07	Rupture	8	0.07	Rupture	6	0.04	Acc. Haem.	1	0.005
Acc. Haem.	7	0.06	Acc. Haem.	3	0.03	Ret. Placenta B.B.O.	6	0.04	Hyperemesis	0	
Ret. Placenta B.B.O.	2	0.02	Ret. Placenta B.B.O.	1	0.009	Acc. Haem.	4	0.04	Ret. Placenta B.B.O.	0	

TABLE II. PRINCIPAL CAUSES OF DEATH (IN ORDER OF FREQUENCY)
Glasgow R.M.H.

1926-30 Total Admissions—19,806			1931-35 22,433		1936-40 23,113			1941-45 21,944		
CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS
Eclampsia	64	0.32	Eclampsia	51	0.23	P.P.H. and Shock	44	0.19	P.P.H. and Shock	37	0.17
Sepsis	59	0.30	Sepsis	35	0.10	Eclampsia	35	0.15	Sepsis	35	0.16
Pl. Praevia	52	0.26	Pl. Praevia	31	0.14	Sepsis	34	0.15	Eclampsia	34	0.15
Pre-eclampsia	43	0.20	Cardiac	31	0.14	Cardiac	29	0.13	Cardiac	24	0.11
Hyperemesis	38	0.15	Acc. Haem.	31	0.14	Acc. Haem.	20	0.09	Ret. Placenta B.B.O.	24	0.11
Cardiac	34	0.17	P.P.H. and Shock	18	0.08	Hyperemesis	19	0.08	Rupture	17	0.075
Acc. Haem.	26	0.13	Hyperemesis	18	0.08	Rupture	18	0.08	Acc. Haem.	14	0.06
P.P.H. and Shock	20	0.1	Pre-eclampsia	16	0.07	Ret. Placenta B.B.O.	17	0.07	Pl. Praevia	12	0.05
Rupture	17	0.09	Ret. Placenta B.B.O.	15	0.06	Pre-eclampsia	14	0.06	Pre-eclampsia	7	0.03
Ret. Placenta B.B.O.	16	0.08	Rupture	14	0.05	Pl. Praevia	12	0.05	Hyperemesis	7	0.03

in the successive quinquennial periods, and, third, how each cause of death is related in percentage to the total admissions.

The majority of maternal deaths comes under three main headings: (1) sepsis, (2) toxemia, and (3) hemorrhage, and Table VII shows a comparison of the percentage of deaths under these three headings occurring during the last ten years in these hospitals and also figures for some other American hospitals, as well as the total percentages for the U.S.A. for 1941.

Let us now examine the main causes of maternal mortality individually and in more detail, to see if improvement has been achieved for each cause, and to attempt to give explanations for such improvement. As sepsis would seem to be the most common cause of death from the U.S.A. figures for the past ten years, and is a common cause in the British Isles as well, I propose to consider this subject first.

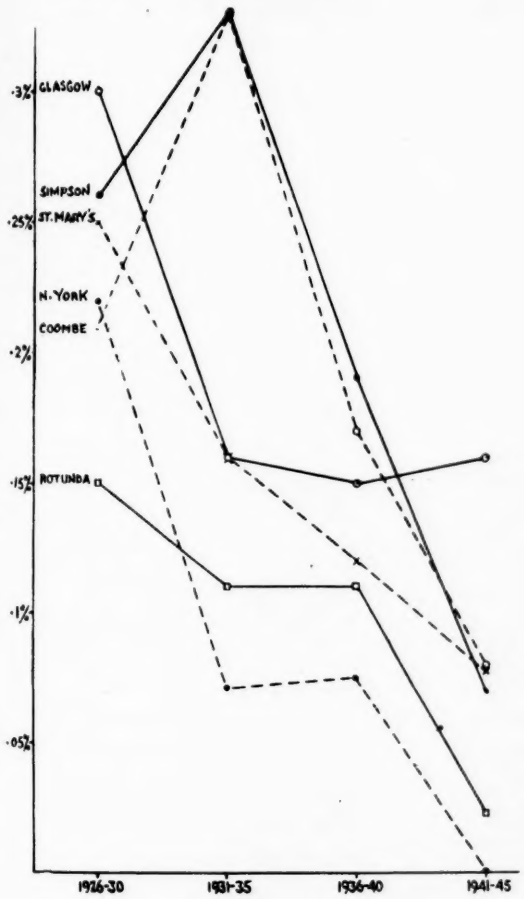

Fig. 5.

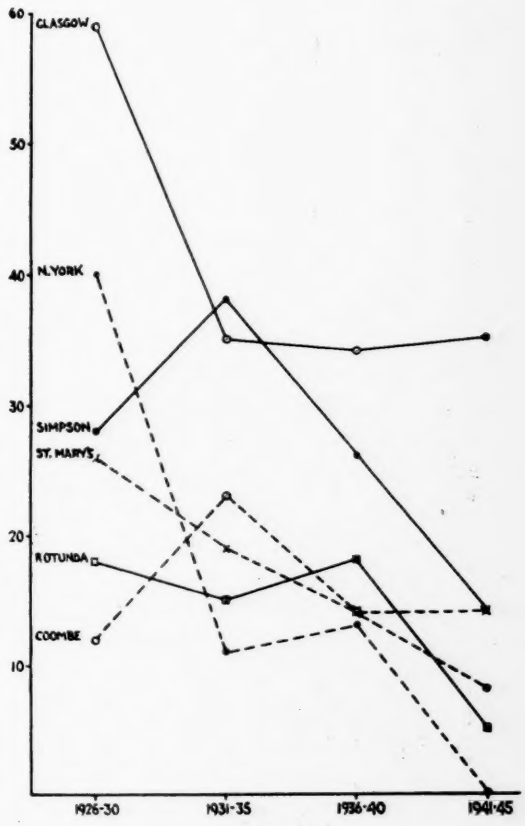

Fig. 5A.

Fig. 5.—Sepsis. Mortality percentage of total admissions for six hospitals.
Fig. 5A.—Sepsis. Number of deaths in six hospitals.

Sepsis

The incidence of puerperal sepsis, as seen from the morbidity graph and Table VIII, has decreased in all the hospitals with the exception of the Rotunda, and the deaths from sepsis have also decreased, with the exception of Glasgow,

TABLE III. PRINCIPAL CAUSES OF DEATHS (IN ORDER OF FREQUENCY)
St. Mary's Hospital, Manchester

1926-30 Total Admissions—10,178			1931-35 11,876			1936-40 11,904			1941-45 18,091		
CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS
Sepsis	26	0.25	P.P.H. and Shock	25	0.21	P.P.H. and Shock	24	0-20	Sepsis	14	0.077
P.P.H. and Shock	26	0.25	Sepsis	19	0.16	Eclampsia	18	0.15	Cardiac	12	0.066
Cardiac	17	0.16	Eclampsia	18	0.15	Pre-eclampsia	17	0.14	Eclampsia	10	0.055
Eclampsia	17	0.16	Cardiac	13	0.11	Cardiac	16	0.13	P. P. H. and Shock	10	0.055
Pl. Praevia	13	0.13	Acc. Haem.	13	0.11	Sepsis	14	0.12	Pl. Praevia	7	0.038
Acc. Haem.	12	0.12	Pre-eclampsia	12	0.10	Hyperemesis	12	0.10	Pre-eclampsia	2	0.011
Hyperemesis	11	0.11	Pl. Praevia	9	0.08	Acc. Haem.	11	0.09	Ret. Placenta B.B.O.	2	0.011
Ret. Placenta B.B.O.	10	0.10	Hyperemesis	7	0.06	Pl. Praevia	6	0.05	Hyperemesis	1	0.006
Pre-eclampsia	9	0.09	Ret. Placenta B.B.O.	6	0.05	Ret. Placenta B.B.O.	6	0.05	Acc. Haem.	1	0.006
Rupture	7	0.07	Rupture	2	0.02	Rupture	3	0.025			

TABLE IV. PRINCIPAL CAUSES OF DEATHS (IN ORDER OF FREQUENCY)
Rotunda

1926-30 Total Admissions—11,914			1931-35 14,245			1936-40 16,900			1941-45 21,351		
CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS
Sepsis	18	0.15	Sepsis	15	0.11	Sepsis	18	0.11	Eclampsia	10	0.047
Eclampsia	13	0.10	Eclampsia	8	0.056	Acc. Haem.	11	0.065	Rupture	6	0.028
P.P.H. and Shock	7	0.06	P.P.H. and Shock	8	0.056	Eclampsia	9	0.053	Sepsis	5	0.023
Cardiac	6	0.05	Cardiac	6	0.04	P.P.H. and Shock	8	0.046	Pre-eclampsia	5	0.023
Pre-eclampsia	5	0.04	Pre-eclampsia	6	0.04	Pl. Praevia	5	0.03	Cardiac	4	0.019
Acc. Haem.	4	0.03	Acc. Haem.	4	0.028	Pre-eclampsia	3	0.018	P.P.H. and Shock	4	0.019
Rupture	4	0.03	Pl. Praevia	4	0.028	Rupture	3	0.018	Acc. Haem.	3	0.014
Hyperemesis	3	0.025	Rupture	2	0.01	Hyperemesis	2	0.012	Pl. Praevia	3	0.014
Pl. Praevia	1	0.008	Hyperemesis	2	0.01	Ret. Placenta B.B.O.	1	0.006	Hyperemesis	1	0.003

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where they have remained pretty stationary for the past fifteen years. It is interesting to note that, though the morbidity rate in the N. Y. Lying-In Hospital is higher than that of our hospitals, there has been no death from sepsis there during the past five years, an achievement which deserves the highest praise. It might be of passing interest to record that, at the Simpson during the year 1936, every patient after delivery received a dose of calcium sulfide, 2 grains, 3 times a day, for four days and during that year the morbidity, which had previously never been lower than 6 per cent (usually between 7 and 8 per cent) dropped to 4.3 per cent. During the following year every patient had prophylactic sulfonamide for three days after delivery and the morbidity dropped further to 3.4 per cent, which was the lowest figure recorded, even though we moved into the new hospital in 1939, until the years 1944 and 1945, when the morbidity has been 2.9 per cent and 2.2 per cent respectively. There is no doubt that the introduction of the sulfonamides has proved of great benefit in reducing the morbidity in all these hospitals. At the Simpson we do not give sulfonamide as a routine now, but if any patient has been liable to infection, then she receives a prophylactic course. This prophylactic practice is believed to have reduced the incidence of sepsis, but if sepsis actually develops, then it would seem that the sulfonamides have not lowered the percentage mortality very appreciably. This is also shown with regard to the other hospitals, with the exception of the Rotunda. (Table VIII.) It is too early yet to know how the discovery of penicillin will affect the incidence and the mortality rate of sepsis, but we are hopeful that its use will lower both rates still further.

Besides the introduction of the sulfonamides, to what other causes may this improvement in morbidity and mortality from sepsis be attributed? The greatest reductions occur in the British, as distinct from the Irish, hospitals, at a time when Britain was in the throes of war, when food was scarce, and many of the cities had suffered greatly from bombing. The people would, therefore, be expected to be undernourished, overanxious, and an easy prey to infection; during the whole period the hospital staffs were severely depleted and overworked and the hospitals grossly overcrowded; a completely aseptic technique was impossible to achieve, owing to the shortage of materials, and, at the Simpson, gloves have not been worn, except for cesarean sections, since 1942, as they were unobtainable in sufficient quantity. It is remarkable, therefore, that, for the years 1944 and 1945, when circumstances were absolutely at their worst, there were only two deaths from sepsis at the Simpson. It is indeed difficult to reconcile these facts, but I think the improvement may have been due to several causes: (1) *Dietetic:* Though the majority of people were underfed during these five years, the mother-to-be was privileged, and she received a pint of milk extra a day, as well as Vitamins A, D, and C, if need be, free of charge. These, of course, were readily obtainable pre-war, but it was only when the pregnant woman realized she was getting something no one else could obtain, and that free if need be, that she really took full advantage of this dietary, which she had never done previously. This helped, to a large extent, to increase the natural resistance to infection. (2) All pregnant women had to visit their doctors or antenatal clinics to get the necessary certificate for the

TABLE V. PRINCIPAL CAUSES OF DEATHS (IN ORDER OF FREQUENCY)
Coombe Hospital, Dublin

1926-30 Total Admissions—5619			1931-35 7010			1936-40 8189			1941-45 9965		
CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS
Sepsis	12	0.21	Sepsis	23	0.33	Sepsis	14	0.17	Sepsis	8	0.08
Pl. Praevia	8	0.14	Pl. Praevia	5	0.07	Cardiac	9	0.11	P.P.H. and Shock	5	0.05
Cardiac	4	0.07	Acc. Haem.	5	0.07	Acc. Haem.	7	0.09	Acc. Haem.	3	0.03
Acc. Haem.	4	0.07	Cardiac	4	0.06	P.P.H. and Shock	7	0.09	Pl. Praevia	2	0.02
P.P.H. and Shock	4	0.07	Eclampsia	4	0.06	Pl. Praevia	6	0.07	Eclampsia	2	0.02
Hyperemesis	4	0.07	P.P.H. and Shock	4	0.06	Eclampsia	5	0.06	Rupture	1	0.01
Eclampsia	3	0.05	Hyperemesis	3	0.04	Hyperemesis	4	0.05			
Rupture	2	0.04	Rupture	2	0.03	Pre-eclampsia	4	0.05			
						Rupture	1	0.01			

TABLE VI. PRINCIPAL CAUSES OF DEATHS (IN ORDER OF FREQUENCY)
New York Lying-In Hospital

1926-30 Total Admissions—17,790			1931-35 14,166			1936-40 17,501			1941-45 19,763		
CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS	CAUSE	NUMBER	PERCENTAGE OF ADMISSIONS
Sepsis	40	0.22	Sepsis	11	0.07	Sepsis	13	0.07	Embolus	6	0.03
P.P.H. and Shock	18	0.10	P.P.H. and Shock	5	0.04	Cardiac	6	0.03	Cardiac	4	0.02
Cardiac	13	0.07	Embolus	4	0.03	P.P.H. and Shock	4	0.024	P.P.H. and Shock	2	0.01
Pre-eclampsia	12	0.07	Acc. Haem.	3	0.02	Cerebro-vasc.	3	0.017			
Rupture	10	0.06	Cardiac	2	0.01	Embolus	3	0.017	Cerebro-vasc.	2	0.01
Eclampsia	7	0.04	Rupture	2	0.01	Acc. Haem.	2	0.012			
Embolus	4	0.02	Pre-eclampsia	2	0.01	Hyperemesis	2	0.012			
Acc. Haem.	2	0.01	Eclampsia	1	0.007	Pl. Praevia	1	0.006			
						Rupture	1	0.006			
						Eclampsia	1	0.006			

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TABLE VII. PERCENTAGE OF THE TOTAL DEATHS, 1936-45

	SEPSIS	TOXAEMIA	HAEMORRHAGE
Simpson	18.2 (25.2)	24.5 (30.7)	19.9 (14.8)
Glasgow R.M.H.	11.7 (10.3)	19.7 (25.2)	30.6 (21.8)
St. Mary's	13.3 (12.2)	22.1 (20.1)	29.2 (27.9)
Rotunda	18.0 (23.3)	23.4 (25.8)	27.3 (19.6)
Chicago Lying-in	39.5	7.4	16.0
Cook County Hospital	23.5	17.6	12.6
N. Y. Lying-In	19.4 (30.9)	4.5 (13.3)	13.4 (16.9)
U. S. A. (1941)	38	25	25
Brooklyn (8 years)	150 cases	110 cases	208 cases

Figures in parentheses indicate previous 10-year (1926-35) percentage.

extra milk and vitamins and also for extra coupons for clothing, mostly for the baby, the milk certificate having to be renewed at frequent intervals; thus every pregnant woman received antenatal care, which many would not have troubled to obtain if there had been no certificates to be signed. This was probably an important factor in decreasing the mortality and morbidity rates in general, but especially with the unbooked cases. (3) As the general practitioners were so overworked, they had neither the time nor the inclination, in many instances, to undertake midwifery, so that, in the main, antenatal care was carried out at clinics, and the patients thus came under skilled observation throughout pregnancy. (4) As nurses were scarce and home helps impossible to obtain, nearly every primipara was delivered in hospital or in a nursing-home; thus the number of infected non-booked cases admitted were reduced. (5) In this connection, also, the effect of the intensive midwifery instruction of the students, which had been carried out for about fifteen years previously, was beginning to bear fruit, and the practitioner realizing his limitations sent the difficult case into hospital, thus avoiding dangerous interference in the patient's own home. This is exemplified from the records, which show that the cesarean section mortality at the Simpson dropped from the previous figure of 3.4 per cent to 1.9 per cent for the last five years. (6) The extended use of the lower uterine segment cesarean section, (7) the more frequent use of blood transfusion, and (8) the better administration of anesthesia; resident well-qualified anesthetists, always available for difficult cases, have undoubtedly played their part. (9) The introduction of Dettol, a most efficient antiseptic for the destruction of the streptococcus; its action on the hands or vulva persists for several hours, and it has been in almost general use in maternity hospitals throughout Britain since 1934. It is used either pure or in a 30 per cent cream; and (10) the very thorough washing of the hands which was insisted upon in the no-glove era, has no doubt also proved effective as well as (11) the insistence on the wearing of masks by all attendants on the woman in labor or in the puerperium. The complete segregation of clean and possibly infected cases, which was possible in 1939, when the new Simpson Pavilion was opened, does not seem to have had such a beneficial effect as was anticipated, for it was only after two to three years' occupation that the morbidity rate decreased appreciably, the figures for the seven years after its occupation being 4.95 per cent, 5.86 per cent, 2.8 per cent, 4.1 per cent, 4 per cent, 2.9 per cent and 2.2 per cent.

TABLE VIII. MORTALITY STATISTICS FOR SEPSIS

	1926-30			1931-35			1936-40			1941-45		
	TOTAL CASES	DEATHS	PERCENTAGE	TOTAL CASES	DEATHS	PERCENTAGE	TOTAL CASES	DEATHS	PERCENTAGE	TOTAL CASES	DEATHS	PERCENTAGE
Simpson	372	28	7.5	486	38	7.8	333	26	7.8	265	14	5.3
Glasgow R.M.H.	1517	59	3.9	2533	35	1.4	1120	34	3.0	901	35	3.9
St. Mary's	1072	26	2.4	989	19	1.9	571	14	2.4	582	14	2.4
Rotunda	433	18	4.1	465	15	3.2	498	18	3.6	617	5	0.8

TABLE IX. MORTALITY STATISTICS FOR ECLAMPSIA

	1926-30			1931-35			1936-40			1941-45		
	TOTAL CASES	DEATHS	PERCENTAGE	TOTAL CASES	DEATHS	PERCENTAGE	TOTAL CASES	DEATHS	PERCENTAGE	TOTAL CASES	DEATHS	PERCENTAGE
Simpson	177	50	28.2	135	15	11.1	150	15	10 (B 5.4)	177	15	8.5 (B 3.4)
Glasgow R.M.H.	395	64	16.2	388	51	15	230	35	15.2	223	34	15.2
St. Mary's	174	17	9.8	129	18	13.9	89	18	20.2	94	10	10.6
Rotunda	60	13	21.7	55	8	14.8	55	9	16.4	86	10	11.6
Coombe	26	3	15.4	34	4	11.8	46	5	10.9	30	2	6.7

TABLE X. MORTALITY IN ECLAMPSIA AND PRE-ECLAMPSIA

	1926-30			1931-35			1936-40			1941-45		
	TOTAL DEATHS	PERCENTAGE OF ALL DEATHS	PERCENTAGE OF ADMISSIONS	TOTAL DEATHS	PERCENTAGE OF ALL DEATHS	PERCENTAGE OF ADMISSIONS	TOTAL DEATHS	PERCENTAGE OF ALL DEATHS	PERCENTAGE OF ADMISSIONS	TOTAL DEATHS	PERCENTAGE OF ALL DEATHS	PERCENTAGE OF ADMISSIONS
Simpson	64	33	0.59	30	17	0.26	28	20.2	0.2	17	20.5	0.09
Glasgow R.M.H.	107	20.4	0.52	77	17.3	0.31	49	15.3	0.2	41	15.2	0.18
St. Mary's	26	12.7	0.25	30	18.3	0.25	35	23.9	0.3	12	15	0.07
Rotunda	18	24.6	0.14	14	20.2	0.1	12	16.7	0.07	15	26.7	0.07
N. Y. Lying-In	19	14.1	0.11	3	10	0.02	1	2.2	0.002		Nil	

Toxemia

DeLee once stated that antenatal care had diminished the incidence of eclampsia, but, as far as the British hospitals are concerned, this reduction has occurred only in Glasgow and St. Mary's, and even they treated 223 and 94 cases, respectively, during the last five-year period. In fact, toxemia still accounts for a large proportion of maternal deaths, both in Britain and the U. S. A., as is shown in my tables. The New York Lying-In Hospital, however, again must be congratulated in so far as it reports only three deaths from toxemia during the last ten years, and none in the last five, and though the Chicago Lying-in Hospital gives almost as good results, yet the death rate from toxemia in 1941 for all the U. S. A. was 25 per cent of all maternal deaths. It is probable, therefore, that DeLee was not far out in his statement, as a large proportion of the cases of eclampsia come in as emergencies, when antenatal care has not been adequate. Only a few occur in patients attending antenatal clinics, and in these cases, the death rate is greatly lowered, viz. 4.4 per cent for booked, against 9.3 per cent for all cases of eclampsia at the Simpson for the last ten years. Be that as it may, the mortality is still appreciable, even in some districts where there is apparently adequate antenatal care. Theobald has pointed out that the incidence of eclampsia shows interesting geographical distribution which makes it difficult to compare different countries' statistics; even in a small country such as Britain, eclampsia is fairly common in the North, and relatively rare in the South. Though the general incidence of eclampsia has disappointingly not altered very much, there has been a decrease in the mortality rate in most of the hospitals, this being especially noteworthy in the Simpson and the Rotunda, whilst the number of deaths has been substantially decreased in Glasgow. This is partly due to improved antenatal care, but I believe that, as far as the Simpson is concerned, the improvement is principally due to the adoption of Stroganoff's method of treatment, and, in the last five years, to the more efficient isolation and nursing which were available in the new hospital, the mortality for this period being the lowest yet recorded, namely 8.5 per cent. At all the hospitals, the percentage mortality from eclampsia related to the total number of admissions has diminished for each quinquennial period, but this has little significance in Scotland, as the total number of cases of eclampsia admitted yearly has not decreased since 1930. These figures would seem to correspond with those of the Boston Lying-in Hospital, where the mortality rate from 1940 to 1944 was 13.5 per cent, which is definitely higher than the Simpson, and slightly lower than Glasgow. It was surmised that the reason there was practically no eclampsia in Germany during the final years of the 1914-1918 War, though it had been prevalent previously, was because the population was on a starvation diet and there was very little consumption of protein. It would seem that this conjecture is fallacious, as the protein available in Britain from 1942 was very small, and yet the incidence of eclampsia has not varied.

One cannot consider eclampsia, however, without also considering pre-eclampsia, eclampsism or profound toxemia without convulsions, call it what you will. If the mortality from eclampsia and profound toxemia are considered

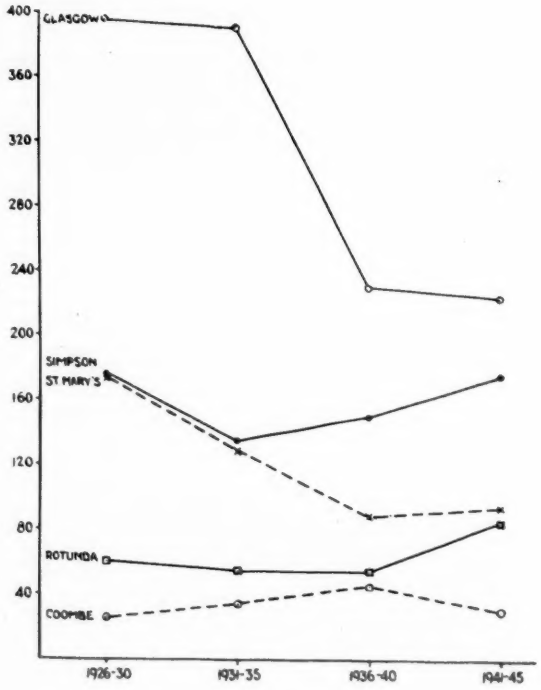

Fig. 6.

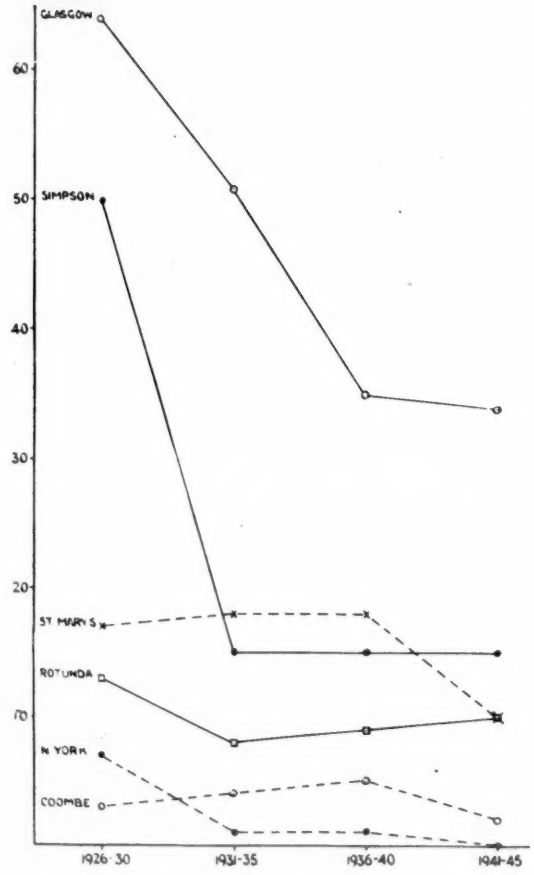

Fig. 6A.

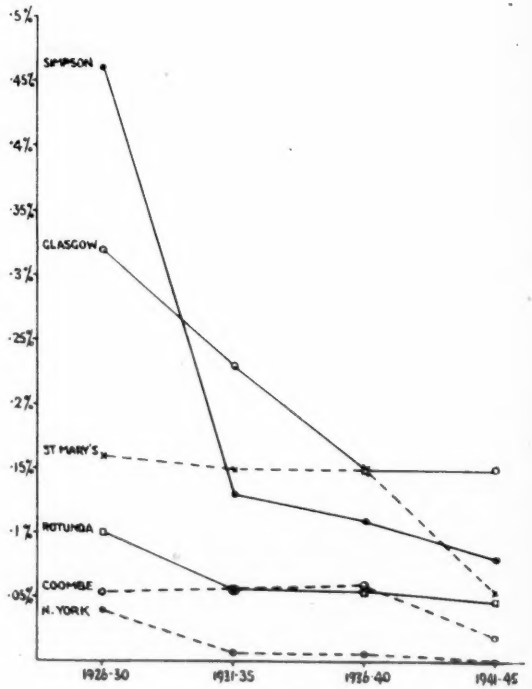

Fig. 6B.

Fig. 6.—Eclampsia. Number of cases in five hospitals.
Fig. 6*A*.—Eclampsia. Number of deaths in six hospitals.
Fig. 6*B*.—Eclampsia. Mortality percentage of all admissions at six hospitals.

together, it will be seen that the mortality has decreased very considerably in all the hosptials with the exception of the Rotunda, where the mortality has remained pretty stationary at about three deaths a year, which number is rather less than in the British hospitals quoted. In order to try and find a cause for this marked decrease in mortality, I have made a detailed study of the Simpson

TABLE XI. PRE-ECLAMPSIA

Mortality Rates and Treatments, The Simpson, 1926-45

	1926-30	1931-35	1936-40	1941-45
Cases admitted	627	712	1107	1592
Deaths	14	15	13	2
Percentage mortality	2.2	2.1	1.2	0.13
Percentage deaths for all admissions	0.13	0.13	0.08	0.01
Treatments adopted—				
Induction labor	125	317	514	672
Cesarean section	10	23	56	88
Abdominal hysterotomy	4	5	15	13
Induction abortion	4	7	7	2

statistics of pre-eclampsia during the twenty years, and it would appear therefrom that the principal reasons are: (1) the increased admission of pre-eclamptic cases, 1592 cases being admitted from 1941 to 1945, as against 627 from 1926 to 1931, due in the main to practitioners' appreciating the treacherous nature of pre-eclampsia and the value of hospitalization to permit of constant supervision, and also to the increased antenatal accommodation in the new Pavilion, which made this ideal feasible; and (2) the increasing number of pregnancies terminated by the induction of premature labor, cesarean section, or even abdominal hysterotomy during each successive five-year period. Eastman and Sheptoe have stated that everlasting vigilance and wary alacrity were necessary if pre-eclampsia was to be managed successfully, and Lazard recommended at the same time earlier termination of pregnancy to improve the results. These opinions are well corroborated by the Simpson figures, for, in the first five years, for 627 cases of pre-eclampsia, 125 labors and four abortions were induced and fourteen abdominal sections were performed, whereas, in the last five years, for 1592 cases of pre-eclampsia, 672 labors and two abortions were induced and 101 abdominal sections were done. By such treatments the mortality from pre-eclampsia has decreased from fourteen deaths (2.22 per cent mortality) between the years 1926 to 1930 to two deaths (0.13 per cent mortality) in the 1941 to 1945 period, and it is impossible to surmise how many cases of eclampsia were prevented. For comparison, Dieckmann reports seven deaths from Chicago during the same five-year period.

The mortality tables show very definitely that one toxemia, which gave great cause for anxiety in the past, namely hyperemesis gravidarum, does not cause the same concern now, Glasgow being the only hospital to show even an appreciable number of deaths during 1941 to 1945, namely seven. In the Simpson there has been no death from this cause during this last period and at St. Mary's there was only one death recorded; even in Glasgow, the total deaths from this cause have dropped from 38 in 1926 to 1930 to seven in 1941 to 1945.

Why has this occurred? From my experience in Edinburgh, I consider that it is due (1) to the early visit to a doctor or clinic, so as to get an extra ration book and clothing coupons, thus bringing the patients under observation much earlier than previously, and (2) to the better instruction of medical students

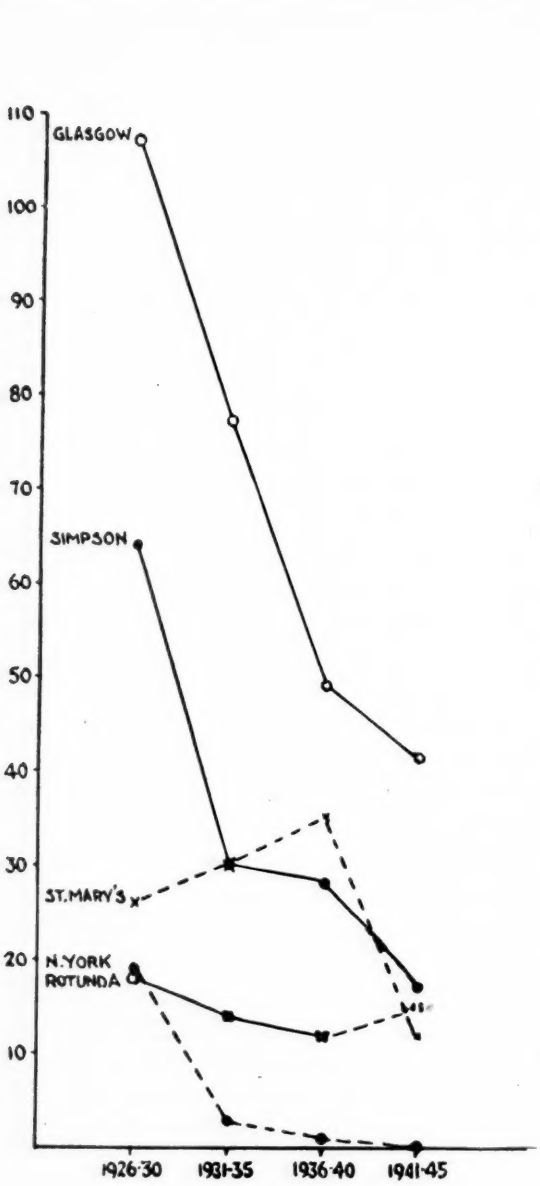

Fig. 7.

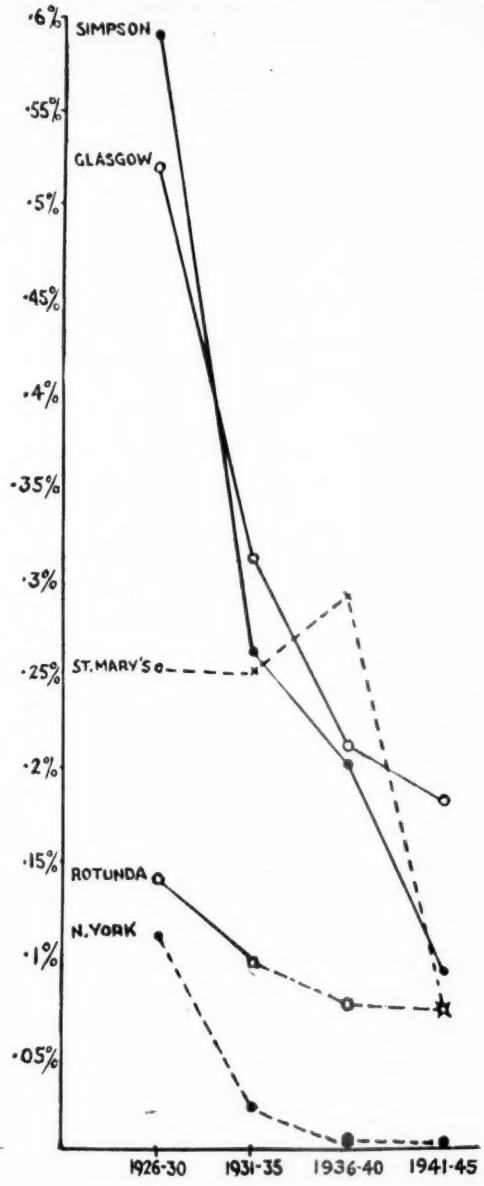

Fig. 7A.

Fig. 7.—Eclampsia and pre-eclampsia. Total number of deaths in five hospitals.
Fig. 7A.—Eclampsia and pre-eclampsia. Mortality percentage of admissions.

as to the significance of vomiting in early pregnancy. They are taught to see their patients early in pregnancy, to inquire about nausea and sickness, and to treat it. If success does not follow domiciliary treatment, the patient is sent to hospital before serious symptoms develop. In the past, patients were seldom

seen early, and if nausea was complained of, this was often made light of by the medical attendant, and no treatment advocated; often, therefore, the patient was not treated adequately until the condition was far advanced. The Simpson statistics show this clearly, as there were 29 toxic cases of hyperemesis treated in 1926 to 1930 with twelve deaths, 43 in the next five years with eight deaths, 62 for the next five years with nine deaths, but only one toxic case was treated and that successfully during the War years. During this period, 130 cases of hyperemesis of moderate severity were admitted, as compared with an average of 290 for the other quinquennial periods. This diminution may also partly be due to the pregnant woman having had plenty to occupy her time and thoughts during the War years and thus the neurotic factor was to some extent eliminated.

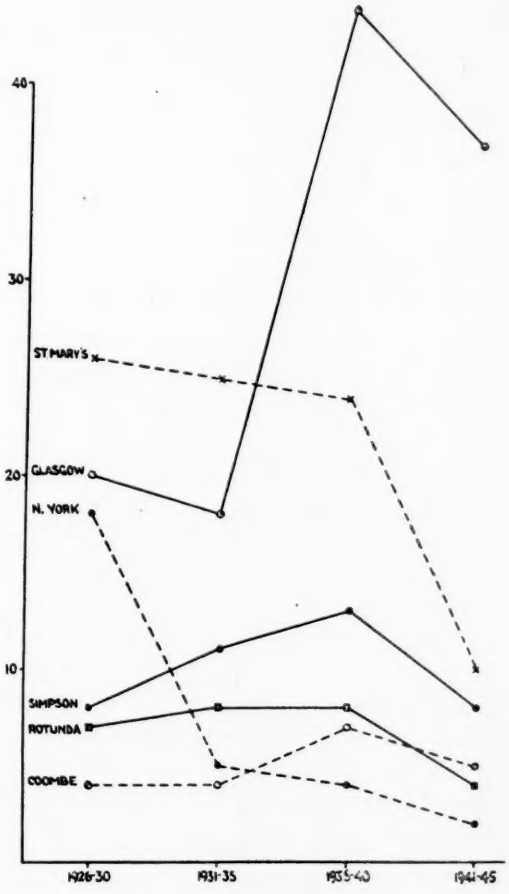

Fig. 8.

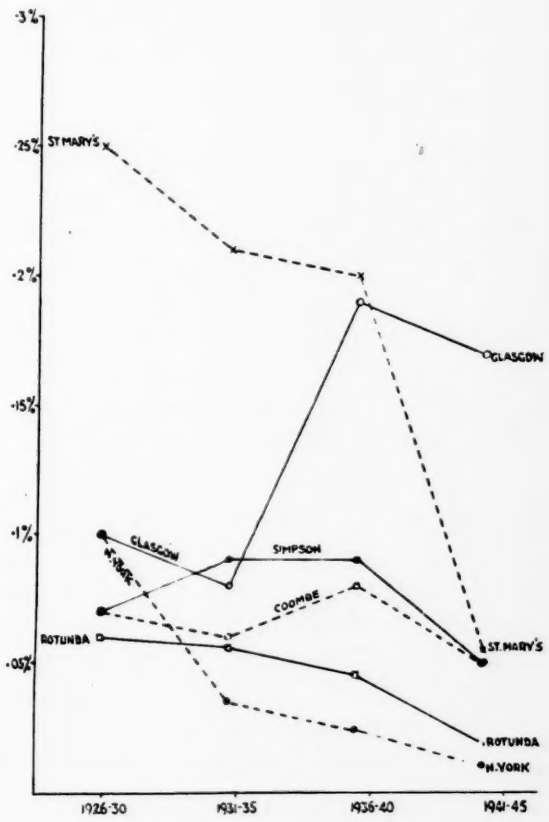

Fig. 8A.

Fig. 8.—Postpartum hemorrhage and shock. Number of deaths in six hospitals.
Fig. 8A.—Postpartum hemorrhage and shock. Mortality percentage of all admissions at six hospitals.

Hemorrhage

Under this heading I have included postpartum hemorrhage and obstetric shock, cases admitted after delivery outside with the placenta still in situ, which

TABLE XII. MORTALITY STATISTICS FOR PLACENTA PRAEVIA

	1926-30			1931-35			1936-40			1941-45		
	TOTAL CASES	DEATHS	PERCENTAGE	TOTAL CASES	DEATHS	PERCENTAGE	TOTAL CASES	DEATHS	PERCENTAGE	TOTAL CASES	DEATHS	PERCENTAGE
Simpson	189	12	6.3	208	11	5.3	214	8	3.9	235	2	0.9
Glasgow R.M.H.	419	52	12.4	490	31	6.3	504	12	2.4	413	12	2.9
St. Mary's	267	13	4.9	233	9	3.9	175	6	3.4	270	7	2.6
Rotunda	103	1	0.9	66	4	6.1	57	5	8.5	153	3	2.0
Coombe	47	8	17	65	5	7.7	81	6	7.4	89	2	2.3

TABLE XIII. PLACENTA PRAEVIA

Results of Principal Treatments at The Simpson

	1926-30			1931-35			1936-40			1941-45		
	TOTAL	MATERNAL DEATHS	FOETAL DEATHS	TOTAL	MATERNAL DEATHS	FOETAL DEATHS	TOTAL	MATERNAL DEATHS	FOETAL DEATHS	TOTAL	MATERNAL DEATHS	FOETAL DEATHS
Plugging with breech	111	6	88	78	9	72	38	2	34	31	0	24
Willett's forceps	2	1	0	36	1	17	46	0	29	47	1	16
Caesarean section	27	1	8	22	0	7	54	1	19	74	1	16

Combined Statistics for 20 Years

					After 35th week		
	TOTAL CASES	MATERNAL DEATHS	PERCENTAGE	TOTAL FOETAL DEATHS	PERCENTAGE	TOTAL CASES	FOETAL DEATHS	PERCENTAGE
Plugging with breech	258	17	6.6	218	84.5	144	104	72.2
Willett's forceps	131	3	2.3	63	48.1	100	32	32
Caesarean section	179	3	1.4	50	28.0	155	26	16.8

I have called retained placenta B.B.O. (baby born outside), placenta previa and, rightly or wrongly, accidental hemorrhage, some of which cases should better be classified under toxemia. By referring again to Table VII, it will be seen that for the British and Irish hospitals, with the exception of the Simpson, hemorrhage has caused the highest proportion of maternal deaths during the last ten years. In Glasgow this is partly due to the number of cases sent in after delivery outside with the placenta in situ, no fewer than 41 deaths being from this cause. This is not the case in the other hospitals, and no such case died in the Simpson from this cause during the last five-year period. Postpartum hemorrhage and shock account for 81 deaths in the Glasgow Maternity Hospital during the past ten years, being the principal cause of maternal mortality, and in St. Mary's they account for 34 deaths, also the principal cause of maternal mortality. In the Simpson, for the same period, the number of deaths from these two causes is 21 and is only the fourth most common cause of death. It is difficult to account for this high mortality, but it is probably due to (1) the admission of almost moribund cases; (2) the necessity for prolonged anesthesia for difficult deliveries for patients admitted as emergencies in far from satisfactory condition; (3) the large numbers of women who have borne 10 children or more who are admitted, whose uteri have lost their power of adequate contraction and retraction. It is possible that the comparatively new method of injection of ergometrine after the delivery of the head may cause a diminution of the number of deaths from this cause, but the treatment is still on its trial in Britain, and it is too early yet to be dogmatic regarding its benefits.

It will be seen from Figs. 9 and 9A and Table XII that the number of deaths from placenta previa has diminished considerably though the incidence of cases has remained fairly stationary. All mortality rates have decreased, and in the Simpson there have been only two deaths from placenta previa during the last five years, and they both occurred in the same year; this gives a mortality percentage 0.9 against 6.3 in the period 1926 to 1930. Can any reason be found for these satisfactory figures? I think it can, by considering the changes in treatment that have been adopted and which are demonstrated in Table XIII. In the earlier years, bipolar version, or plugging with the half breech, was the prevalent treatment and accounted for a high mortality rate, whereas, in the succeeding years, it was performed less and less frequently and the death rate improved. Contrariwise, cesarean section was carried out for only a few cases in the earlier years, but in the later years it was performed more and more frequently, and was associated with a low mortality rate. Also, in place of plugging with the half breech, with or without version, Willett's forceps came to be more frequently applied, having almost as low a maternal mortality rate as cesarean section. The use of Willett's forceps has been decried by some authorities and I have read many papers by United States authors deprecating their use; perhaps, therefore, I might be allowed to emphasize the good results that have been obtained by their employment in selected cases. As will be seen from my figures, the maternal mortality is low, though the fetal

mortality compares unfavorably with that of cesarean section. I would suggest, therefore, except in cases of marginal placenta previa, when rupture of the membranes alone suffices, if cesarean section is not indicated or advisable, that the application of Willett's forceps to the scalp of the child gives both mother and child the best chance of survival, and that there is a definite place in obstetrics for their use.

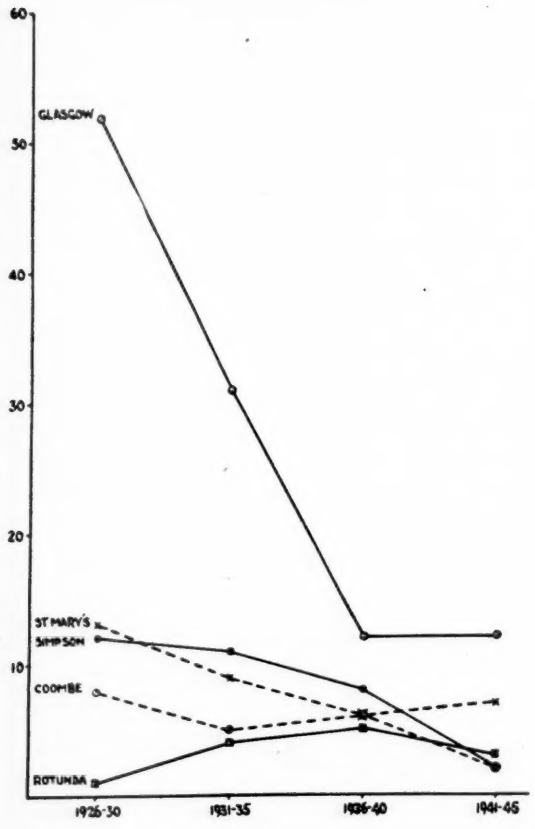

Fig. 9.

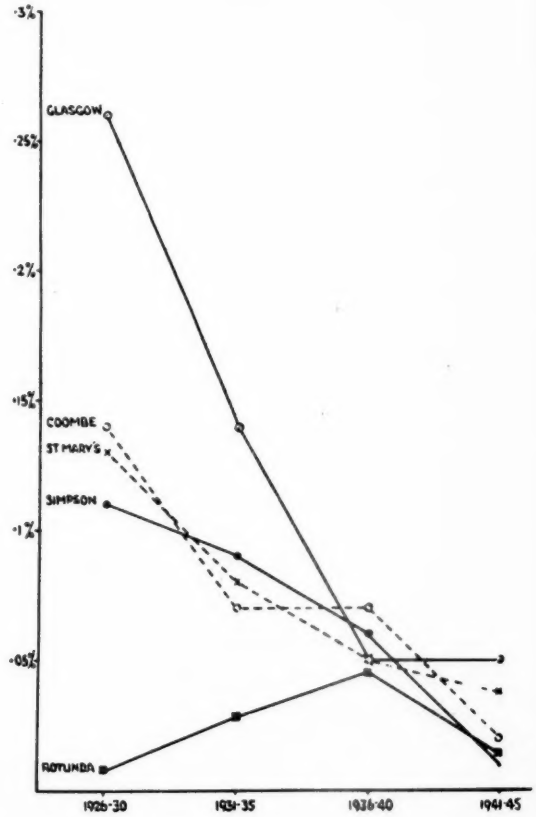

Fig. 9A.

Fig. 9.—Placenta previa. Number of deaths in five hospitals.
Fig. 9A.—Placenta previa. Mortality percentage of all admissions at five hospitals.

In my opinion, the greatly lowered mortality in cases of placenta previa is due to three main reasons: (1) the adoption of cesarean section for the more dangerous types and the use of Willett's forceps, when indicated, in place of plugging with the half breech, (2) the almost routine use of blood transfusion as a prophylactic against the effects of possible dangerous blood loss and also as a replacement for any great loss, and (3) the fact that students have been taught that any case of bleeding in the last three months of pregnancy must have immediate hospitalization and be examined only by an expert; the high mortality in the earlier years was partly due to examination being carried out in the patient's house, excessive bleeding being caused and the patient being sent to hospital in extremis.

In some hospitals, notably in Glasgow, a number of cases are admitted with retained placenta, but these numbers are being diminished by the more frequent use of a flying squad of efficient personnel fully equipped with plasma and blood, so that the patients may be adequately treated in their own homes, and their condition rendered satisfactory before transportation to hospital. This again has involved the better instruction of students so that they are made to realize that the safest way to treat these patients is not to move them until shock and blood loss have been dealt with. It is pleasing to record that the Simpson, which provides such treatment, has had no deaths from retained placenta during the last five years.

The incidence of accidental hemorrhage as a cause of maternal death has diminished very considerably, the only hospital in which the mortality is appreciable from 1941 to 1945 being Glasgow, where they had fourteen deaths, whereas at the Simpson and St. Mary's, only one death was recorded at each. This improvement is again partly due to better tuition, by a better understanding of the pathology of the condition, and thus to more efficient treatment. Nearly all such cases are now treated expectantly, and cesarean section with or without hysterectomy, which used to be carried out frequently for the concealed variety, is now practically never required. The improvement is also due to the more efficient antenatal supervision of all cases of pre-eclampsia and especially those with marked hypertension. Thus once again a one-time dreaded disease can now be regarded with a degree of equanimity.

Failed Forceps Outside

Before discussing the future I would like to prefer to another important cause of mortality in hospitals admitting non-booked cases, namely the so-called F.F.O.s—failed forceps outside—where the practitioner has tried to deliver with forceps, but, having failed to do so, sends the patient to hospital.

Quite an appreciable number of deaths in Glasgow, St. Mary's, and at the Simpson have occurred in such cases, especially where there had been gross interference before admission. The causes of death are shock, obstetric or anesthetic, sepsis, or, in a few cases, rupture of the uterus. The improvement achieved in dealing with such cases is illustrated in Figs. 10 and 10*A*. I consider that this improvement is due again to (1) better tuition of students, (2) more adequate antenatal care, so that cases likely to develop dystocia are recognized, and arrangements made for their delivery in hospital, and (3) improved methods of treatment in hospital, e.g., lower segment cesarean section, blood transfusion, anesthesia, etc.

What of the Future?

From the statistics that I have just put before you it will be appreciated that midwifery practice has improved in the last twenty years; the best results are obtained in the hospitals admitting few if any emergency cases, except from their own district cases, which latter are supervised by the hospital antenatal clinics. There is still room for improvement, especially in the standard of domiciliary midwifery without the aegis of the hospital antenatal clinics, so

that potential difficulties are recognized early and their unsuitability for domiciliary care realized; thus will serious emergency admissions decrease, and the few that are not foreseen will arrive in hospital in better trim and without trauma. How can this be achieved? This is a very important consideration and especially so is it in Great Britain, where we are approaching a new era in the practice of medicine, with the advent of a National Health Service, which includes midwifery and is due to start on July 5, 1948. It is the duty of the obstetricians therefore to advocate a scheme, which, if carried out efficiently and conscientiously, will give Britain, despite its large and crowded industrial centers, a chance of producing the lowest mortality, morbidity, and infant mortality rates in the world. My suggestions for future improvement are as follows.

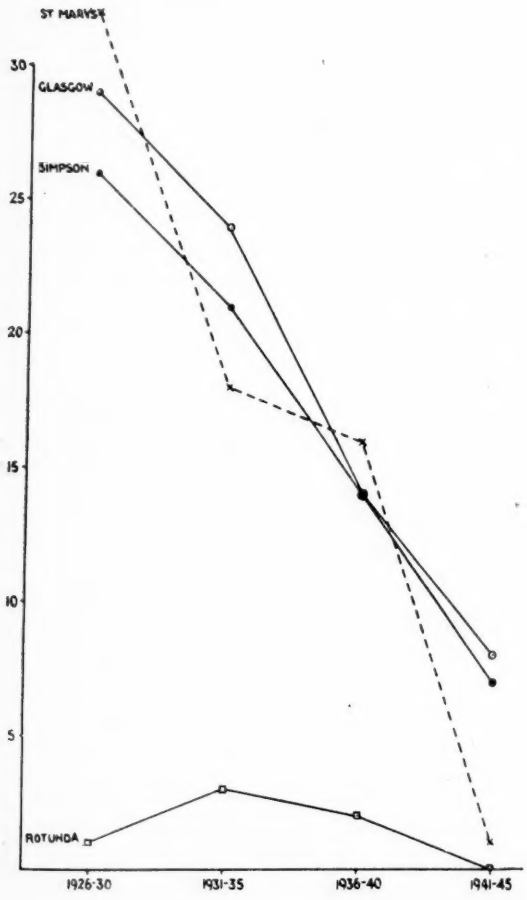

Fig. 10.

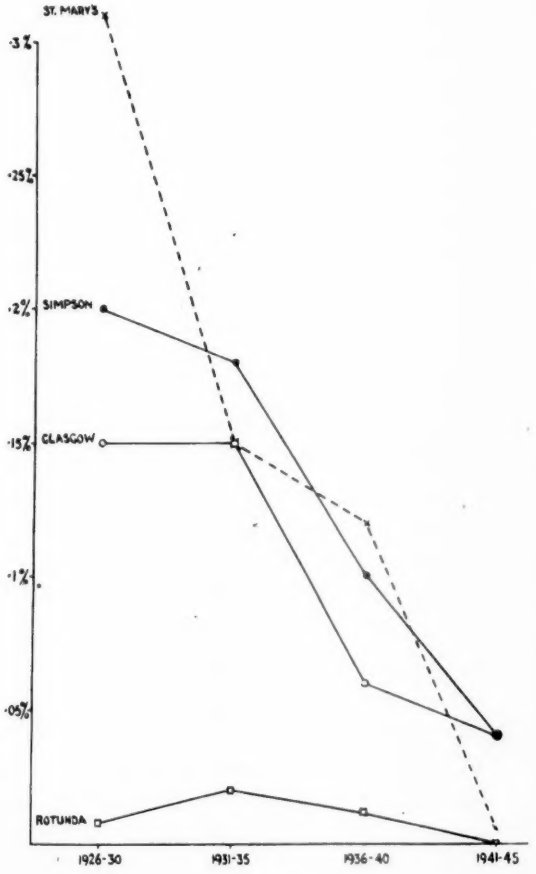

Fig. 10A.

Fig. 10.—Failed forceps outside. Number of deaths in five hospitals.
Fig. 10A.—Failed forceps outside. Mortality percentage of all admissions at four hospitals.

Adequate and Efficient Antenatal Care for All Pregnant Women

The importance of efficient antenatal care can be gauged by noting the disparity between the mortality percentage amongst the booked cases, i.e., those who have attended at least two antenatal clinics (a very low criterion) and the total mortality percentage of all cases admitted both booked and unbooked as

already remarked upon (shown for the Simpson in Fig. 2). The statistics of the New York Lying-In Hospital would seem to afford an excellent example of how efficient antenatal care for the hospital and surrounding district can lower the mortality to almost an ideal minimum.

Though antenatal care has progressed out of all knowledge during the last thirty years, it is still far short of being ideal, and I would suggest that improvement could be achieved under the following headings:

(a) *Personnel:* The responsibility for antenatal supervision must devolve on those with some extra postgraduate training in midwifery, which experience alone can make them conversant with its numerous problems and pitfalls. The undergraduate standard of instruction is only sufficient to permit of practice under supervision.

(b) *Antenatal Clinics:* The large clinics, which are so common in Britain at present, owing to the increasing number of antenatal patients, should be abolished. What clinic can see and examine efficiently 200 or more patients in an afternoon? These clinics should be more individual, the patient being seen by the same doctor at each visit, so that each case can be followed up satisfactorily, and a personal interest taken. This would greatly help the patient's comfiture and confidence and would be advantageous when slight abnormalities, which might escape notice by a new examiner, made their appearance. No session should be longer than two and a half hours and no individual doctor should undertake the examination of more than 25 cases in that time.

(c) *Accommodation:* There must be adequate antenatal in-patient accommodation, with (1) sufficient nursing and medical personnel for all patients requiring hospital supervision and treatment, such as those suffering from toxemia, cardiac disability, diabetes, antepartum hemorrhage, pyelitis, or mere debility, etc. The first antenatal bed in the world was provided at the old Simpson Memorial Hospital in 1899 by one of your Honorary Fellows, the late J. W. Ballantyne, the pioneer in antenatal care, but it was not until 25 years later that an antenatal ward came into existence, and it had only ten beds. When the new Pavilion was erected in 1939, it was thought that 25 per cent of the total beds should be devoted to antenatal cases, and approximately 30 beds were given over for such cases. This has been found to be entirely insufficient and it would appear that about 40 per cent of the total beds in a maternity hospital should be devoted to antenatal cases, the exact proportion depending on the character and working conditions of the population in the area which the hospital serves. (2) Sufficient lying-in accommodation must also be provided for all cases regarding the difficulty of whose confinement there is any doubt. This would include all primiparas and multiparas who had had nine previous confinements, besides patients with slight contraction of the pelvis, with history of previous difficult labors or stillbirths, etc.

Teaching

There must be more practical and clinical training of students or of young graduates, who are going to undertake midwifery in their general practice.

I agree wholeheartedly with H. M. Little, who, in his presidential address

to the Canadian Medical Association in 1924 on the Progress of Obstetrics in the preceding 25 years, stated, "Antenatal care by itself is hopeless without some improvement in the teaching and practice of obstetrics. The most recent graduate is no more capable of undertaking any but the simplest midwifery cases than he is to practice abdominal surgery," and concluded by advocating better training for students and special training for men in large centers, who aim at becoming specialists. Undergraduate training in midwifery in Britain has made great strides in the last twenty years, but the average graduate is still allowed to go into general practice badly equipped in practical experience though his theoretical knowledge may be satisfactory.

I would suggest, therefore, that every doctor who wishes to make midwifery part of his general practice and will therefore be undertaking antenatal examinations should have three to six months' intensive experience in practical midwifery, including antenatal and postnatal care, residing in a maternity hospital, before he is allowed to practice midwifery. An extra degree, such as a B.Obst. or B.A.O., could be given to these graduates, which would give proof of their experience and status to practice general practitioner midwifery. This would ensure not only that efficient antenatal care would be afforded but also that the practitioner would be able to recognize and assess the severity of abnormal conditions occurring during labor; he would realize if a condition was beyond his resources or capabilities and would send the patient to hospital early, not interfered with and in much better trim, and without trauma. Thus the failed forceps case, instead of being a common cause of mortality, would become more and more a relic of the past, and many lives would be saved thereby.

Compared with these two fundamental factors, my other suggestions are of minor significance, but I think if practiced would aid the progress of midwifery.

Blood Grouping

Every pregnant woman should be blood grouped and her Rh factor taken. This would seem to be as important, if not more so, than the routine Wassermann reaction. Such a procedure would save fatalities following transfusion which, unfortunately, are by no means rare, and would also accelerate reliable transfusion in urgent cases.

Flying Squads

Flying Squads, fully equipped, should be immediately available night and day in order to deal with cases of hemorrhage and shock and retained placenta occurring in the area served by the hospital and should be at the service of all practitioners in that area who required their aid. As has been already noted, this would save a number of lives and prevent cases being transferred to hospital in a collapsed and often moribund condition.

Hospital Construction and Administration

Besides adequate accommodation already mentioned for antenatal cases, there must be efficient administration to prevent the spread of any infection in the hospital: (1) Patients should be delivered each in a separate room, and

the big labor ward, which was once so common, must be abolished. (2) Emergency cases admitted during labor must be isolated efficiently from the so-called booked or clean cases; they should be delivered in entirely separate labor rooms, which should be disinfected after each case, and if single rooms are not available for all such cases for the puerperium, the wards should have few beds and be well-aired; there should be, however, sufficient single rooms for the frankly or likely septic cases. (3) There should be an entirely separated ward, or preferably, block for cases of abortion; they should be completely isolated from the puerperal patient whether clean or suspect, and their treatment should be carried out in a separate theatre. This has been rarely possible in Britain, and the admission of abortions to maternity hospitals, besides often raising the mortality rate, may be a potential cause of increased morbidity.

Penicillin and Possibly Other Therapeutic Agents

Great improvement has been effected in lowering the morbidity rate and the number of deaths from sepsis by efficient technique and hospitalization and by the administration of the sulfonamides, both prophylactically and curatively. What further improvement may follow the extended use of penicillin? It is as yet too early to speak definitely on this point, but the prospect seems hopeful. Also, may there not be some new preparation round the corner, soon to be discovered, which may prove to be even more potent than either? And, last, what a niche in obstetric history awaits the man or woman who discovers the cause of pre-eclampsia and eclampsia, for once the cause is discovered, specific treatment or, better, the knowledge of its prevention will surely follow at no far distant date, and another common cause of maternal mortality will be conquered.

BENIGN TROPHOBLASTIC CELL PROLIFERATION*

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WHENEVER an invasion of the uterine wall by trophoblastic tissue occurs, two possibilities may be present: benign trophoblastic cell hyperplasia or a form of chorionepithelioma. Since differentiation between the two conditions is based quite often on a matter of opinion rather than definite histologic criteria, many uteri are sacrificed needlessly.

Many observers have noted that trophoblastic cells may invade the uterine wall in normal gestation. According to Marchand[1] the process is not a casual one, but it serves the purpose of firmly anchoring the implanted ovum to the uterine wall. The amount and extent of this cellular infiltration vary considerably; it increases up to the sixth month, to disappear almost completely toward the end of pregnancy. In only a small number of cases, the infiltrating cells invade the blood vessels, with subsequent formation of pulmonary emboli. Schmorl[2] found that this occurred in 80 per cent of 150 eclamptic cases studied at autopsy. His conclusions were based on the presence of scars in the pulmonary tissue which he claimed to be the end result of absorption of previous trophoblastic cell emboli.

Moreover, many authors who have examined uteri with adherent moles or placental tissue have remarked on the amazing depth of invasion of the villi into the uterine musculature. The early literature lists this finding under the term of placentary polyp. It has been suggested that the aggressive tendencies of these trophoblastic cells are kept in check by a restraining factor, syncytiolysin, which is produced by pregnant uterus. In favor of this mechanism, Frankl[3] has shown that the serum of normal pregnant women has solvent properties on these embryonal cells in vitro; the serum from pregnant women with chorionic epithelial tumors does not contain this solvent action. Other observers have not been able to demonstrate this syncytiolysin. Of late it has been thought that a disturbed lutein function accounts for the excessive trophoblastic growth.

As far back as 1898, Ruge[4] stressed the point that as long as the chorionepithelial cells (at his time interpreted as of decidual origin) are still connected with the villi, it is proper to speak of proliferation and not of new growth, the latter term implying a kind of independent cellular life. This conception of independent life and aggressiveness which applies to any cellular proliferation elsewhere in the body does not apply, however, to the growths under consideration, invasiveness and obliteration of neighboring structures being inherent to the normal implantation of the ovum into the uterine wall. The absence of a sharp line of demarcation between normal and pathologic growths requires special notice, because it is just in border-line situations that difficulties may arise. These difficulties are clearly reflected by the disparity that still exists in the statistics on the actual frequency of chorionepithelial growths.

Velits[5] is credited with the first attempt to differentiate chorionepithelial cell proliferation into a benign and a malignant form utilizing histologic criteria. The absence of mitotic figures, the predominance of wandering cells, and extensive tissue necrobiosis—these factors were indicative of the harmless growths. In actual practice, this information could not be obtained unless the uterus was already removed.

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More important progress was made by Marchand[1] who, in a series of articles from 1895 to 1903, was able to demonstrate that the "deciduoma malignum" of Sänger was derived from chorionic epithelium, from which both typical and atypical growths might occur. Typical chorionepithelioma he called that characterized by the presence in varying proportions of small, polyhedral, pale-stained cells with intimate cytologic characteristics of Langhans' cells and of large multinucleated plasmodial masses simulating the syncytial buds of the villi, these two cell types together giving rise to a well-defined structure closely resembling the epithelial cover of villi in early stages of placentation. He termed atypical chorionepithelioma that in which the Langhans' cells were missing and only giant syncytial cells could be recognized in the growth. Although Marchand did not claim any striking difference in the clinical course between the two types of growths, the typical and the atypical, a few years later Schmauch,[6] after careful review of 206 cases, concluded that Marchand's atypical forms were provided with much less aggressive potentialities than the definite malignant forms. He also recognized a transitional type, of intermediate malignancy, "composed chiefly of elements like syncytial cells, assembled in groups, as well as syncytium and Langhans' cells." According to Schmauch, while, in the typical forms, the structural patterns compared with those found in early stages of pregnancy, in the atypical ones they resembled more closely those found in the puerperal uterus. In his opinion, prognosis depended mainly upon the abundance of the most aggressive cellular type, the cell of Langhans. This assumption was based on Langhans' theory that the chief part in the embedding of the villi was played by the Langhans' cells, not by the syncytial cells as thought by Marchand; hence, his conclusion that the more numerous the Langhans' cells, the worse the prognosis; conversely, whenever evidence of syncytial change in the Langhans' cells and of transformation of syncytium in the syncytial cells prevailed in the growth, the outlook for the case was more favorable.

Schmauch paved the way for Ewing's[7] masterful study of the problem. Although not denying that the syncytial wandering cells of the atypical chorionepithelioma of Marchand are capable of multiplying, Ewing considered it unlikely that these cells could be able to develop into a progressive malignant tumor. After stressing the point that definite syncytium, Langhans' cells, and villi are missing in the growth, and that the cases exhibiting budding syncytium and Langhans' cells must be rigidly excluded from the group under consideration, he concluded that the so-called atypical chorionepithelioma was a "productive inflammation," a "mixture of degeneration with proliferation" accompanied by thrombosis of blood vessels and tissue necrosis; hence his proposal to term the process "syncytial endometritis," clearly indicating the true essence and harmless nature of the process.

For another type of transitional lesion in the chorioma group, he proposed the term "syncytioma or syncytial chorioma." This tumor is not made of just isolated cells, as in syncytial endometritis, but is composed of sheets or masses of giant syncytial wandering cells. Langhans' cells might be present in this type of growth, but they are an inconspicuous feature, and they fail to reveal any evidence of hyperplastic or anaplastic tendencies. Instead, the wandering cell plays the role of invader, but capable of producing a tumor of only limited aggressive potentialities. This tumor progresses for a while, then loses its power of further expansion, and then undergoes a process of regression.

This work of Ewing sheds considerable light on the so-called cured cases of chorionepithelioma previously reported in literature. Velits[5] collected eight cases of chorionepithelioma which completely recovered after curettage. More likely these were cases of syncytial tumors of Ewing rather than true chorionepithelioma. The same is probably true of the two cases of Proust and Bender,

those of Noble, Fleischmann, Cazin-Segond, Kolomenkin and Hormann (discussed in Ewing's paper), and more recently of the nine cases of Vineberg,[8] eight of which completely recovered following hysterectomy. The latter attributed his excellent results to early diagnosis, but one wonders if they did not belong to the syncytial group. Rosenzweig[9] raised the same question in the chorionepithelioma reported by Ferguson.[10]

In line with Ewing's nomenclature, Geist[11] has reported four cases; two belong in the "syncytial endometritis" group and two in the "syncytioma" class. Similarly, Rosenzweig has reported one case in each group. The three cases of Greenblatt and Pund,[12] each exemplifying a condition of syncytial endometritis, syncytioma, and of exaggerated syncytial reaction following an abortion, were so diagnosed and treated conservatively. A case similar to the last one of Greenblatt and Pund was reported by Choisser and Notes.[13] They attributed the endometrial reaction to the combined effects of hyperestrinism, low-grade infection, and to trauma produced by the long-continued use of a metal-stem pessary.

In the series of 200 cases of hydatidiform mole collected by Hertig and Sheldon,[14] nine were diagnosed as "syncytial endometritis." They placed them in Group VI among the malignant moles. They were placed in the malignant mole group because of the invasive character of the trophoblastic cell proliferation. Yet, of these nine cases, two patients were alive and well seven months and four months, respectively, with their uteri intact after removal of the mole only. Of the other seven, submitted to hysterectomy, one died postoperatively of peritonitis, and the remaining six were all alive and well three months to nine years later. It is apparent, as the authors pointed out, that these nine cases, despite their threatening morphologic structure, did not constitute a true chorionic malignancy. These authors also present another case, that of a woman who passed a mole which appeared to be malignant upon microscopic examination. A curettage done on the sixteenth postpartum day yielded a few myometrial fragments from the placental site, displaying patterns consistent with a diagnosis of syncytial endometritis. A hysterectomy was advised but refused by the patient, who, after four years, is still living and well. This and other similar cases show that the usual morphologic criteria of malignancy universally observed in grading tumor growth are not strictly applicable to trophoblastic cell proliferation.

In light of the above experiences it becomes apparent that only through the follow-up of cases carefully studied pathologically can proper evaluation be gained in ascertaining the necessary operative interference.

Report of Cases

CASE 1.—The patient, a 22-year-old white woman, was admitted to this hospital with a history of vaginal bleeding of two days' duration, which had started after a two months' period of amenorrhea. She had always had regular menses, with no bleeding in between periods. Family and past history were irrelevant. Examination at admission revealed a well-nourished young woman. Findings in the chest and abdomen were completely negative. A vaginal examination was made, and it revealed a patent, softened cervix from which a good deal of blood was issuing. The impression was of a threatened miscarriage and, as bleeding was continuing, a curettage was performed.

At curettage, the surfaces of the uterine cavity were found to be somewhat thickened and lined by a firm tissue, grayish-pink in color, which did not have the usual gross characteristics of placental tissue.

Microscopic examination of the curettings showed a thickened endometrium, spongy in appearance, due to marked hypertrophy and tortuosity of glands. The latter presented pronounced saw-tooth convolution and scalloping, and were lined by a low, pale-stained and

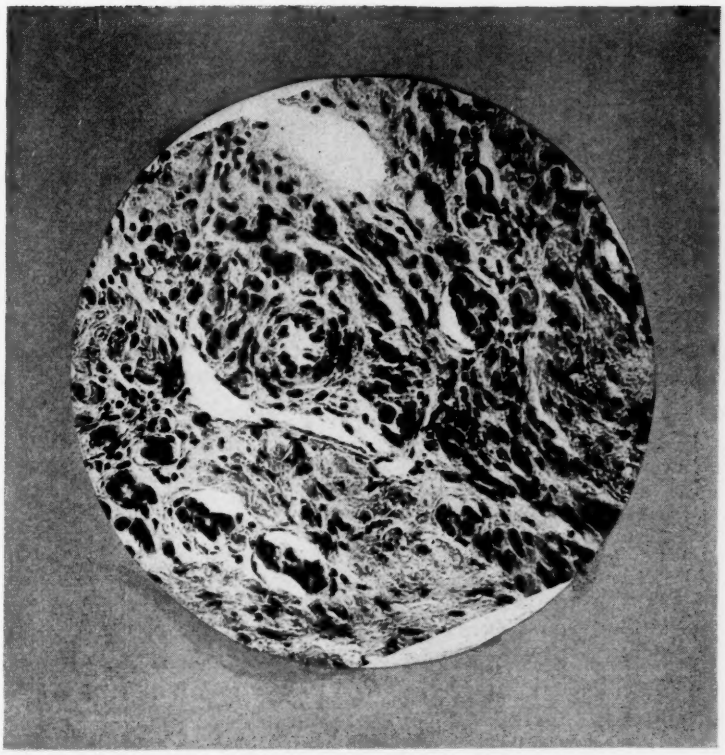

Fig. 1.—Deep invasion into the myometrium of atypical trophoblastic cells, either sparse or in large sheets. Cells identical in type are noticeable in the lumen of thin-walled hematic channels. (Case 1—Microsc. Zeiss—Oc. 10—Object 10.)

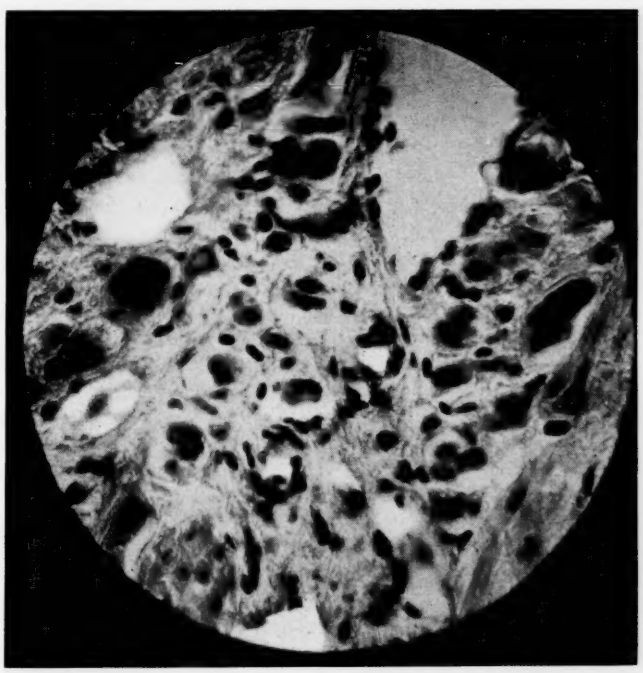

Fig. 2.—Oddly shaped, deeply stained, not distinctly bounded trophoblastic cells infiltrating the myometrium. (Case 1—Microsc. Zeiss—Oc. 10—Object 40.)

actively secretory epithelium with a frayed-looking edge suggesting melting-down of cytoplasm. The superficial endometrial layers showed patchy necrobiotic changes, with poor staining of cellular structures and imperfect cell differentiation. A rather massive infiltration of leucocytes, chiefly polynuclear, numerous mononuclear clasmatocytes, and a good many extravasated red blood cells were noticeable in these degenerated areas, together with interglandular stroma extremely rich in cells, which were larger than the usual endometrial stroma cells, round or polygonal in shape, with a wide zone of cytoplasm surrounding the nucleus. These cells, with characteristics of decidual cells, were arranged in mosaic-like fashion and appeared to be most numerous where the glandular elements were few.

Elsewhere a few chorionic villi were recognizable; they seemed to have undergone advanced regressive changes, as shown by the poor staining and imperfect cell differentiation, with partial or complete hyaline degeneration. The epithelial covering of the villi was missing in some areas, hyperplastic in some other areas. Where the structure was better preserved, it appeared to be composed of cells of various size and shape, some large and some small, some polyhedral, some others round or elongated or bizarre-shaped. All these cells were characterized by a deeply stained, irregular nucleus surrounded by abundant acidophilic cytoplasm. Cells identical in type, either sparse or in large sheets, were scattered in the decidual tissue and deeply infiltrated fragments of myometrium obtained at curettage. (Fig. 1.) The cells within the myometrium showed a tendency to fuse together into plasmodial masses, and as they fused together, the nucleus and the cytoplasm stained deeper, and in their coloring and structure they resembled syncytial cells. In other areas these cells grew to gigantic proportions, giving rise to oddly shaped, deeply stained and not distinctly bounded cells which were especially numerous in the proximity of thin-walled intramyometrial blood vessels. (Fig. 2.) Cells identical in type were noticeable at times in the lumina of the vessels themselves. As these cells penetrated in the depth of the myometrium they seemed to lose the polyhedral or round shape that they displayed in the decidual tissue and often assumed a spindle form, so that it was difficult to differentiate them from connective tissue cells, the fundamental difference being their greater affinity for stains. Despite the evident cellular aggressiveness, with invasion of blood vessels, deep infiltration, and spreading apart of muscular fibers, no mitotic figures could be recognized. The intervening muscular structures showed patchy regressive changes with loss of striations and hyaline changes which increased in severity with the increase of the cellular infiltration.

Our final impression was that the picture was not unlike that ascribed to the so-called atypical chorionepithelioma. The provisional diagnosis was syncytioma, but, as we were undecided as to real malignancy of the process, a decision was made to treat the patient expectantly.

Following curettage, two gonadotropic hormone tests were performed two weeks apart and both yielded negative results. At the end of one month a second curettage was done, and, amazingly, the general appearance was found to be that of a normal endometrium in the secretory stage of the menstrual cycle. No plasmodial cells or any other structural or cellular atypism could be recognized, and the fragments of myometrium obtained at curettage were found to be free from cellular infiltration. The patient made an uneventful convalescence and she is now perfectly well, and in the fourth month of a normal pregnancy.

CASE 2.—The patient, a 19-year-old white woman, was admitted to this hospital with a moderate amount of vaginal bleeding, which, according to the history, had started about two months before and since then had persisted off and on, after a two months' period of amenorrhea. During this period she had noticed swelling of the breasts, and had suffered with frequency and nausea. The family and previous personal history were irrelevant.

Examination on admission showed a well-developed and well-nourished young woman with no physical complaints except for the vaginal bleeding. Vaginal examination revealed an enlarged uterus, about the size of a two and one-half to a three months' pregnancy. The external os was completely closed. The patient was kept four days under observation, with no particular treatment except bed rest. The bleeding quieted down somewhat, so that, on the fourth day, she was discharged, with the advice that she should return if bleeding should start again. Diagnosis on discharge was threatened miscarriage, probably inevitable.

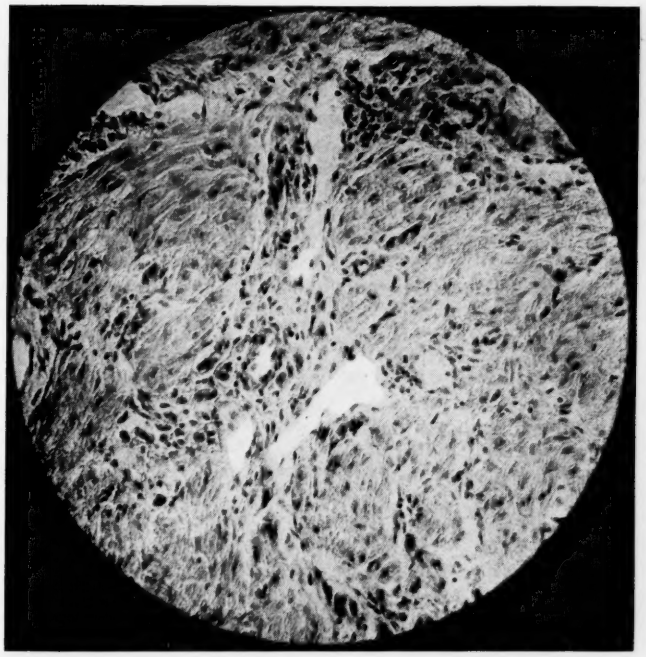

Fig. 3.—Large sheets of cells with characteristics of Langhans' cells and occasional larger cells in syncytial arrangement infiltrating and spreading apart the muscular bundles of the myometrium. (Case 2—Microsc. Zeiss—Oc. 10—Object 10.)

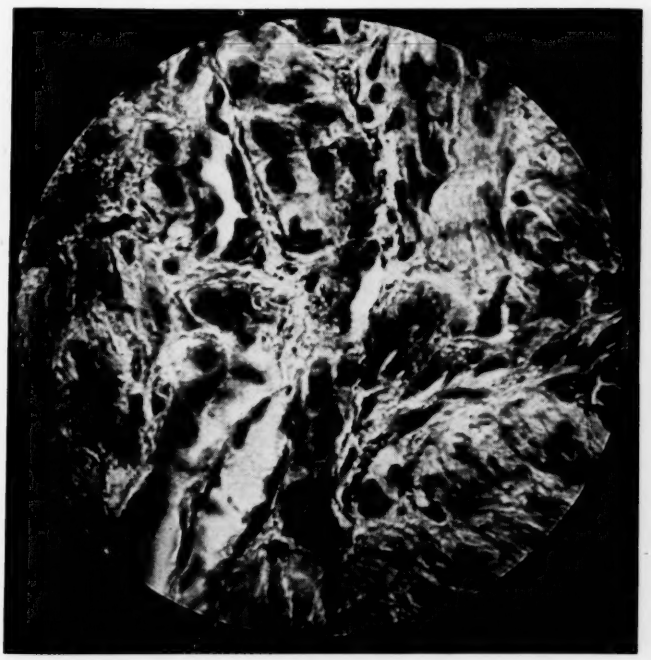

Fig. 4.—A view at high magnification of the infiltrating trophoblastic cells represented in Fig. 3. (Case 2—Microsc. Zeiss—Oc. 10—Object 40.)

She was readmitted 22 days later with a slight amount of vaginal bleeding and intermittent abdominal cramps. The day of admission she passed a fetus, two inches in length, and some shreds of placental tissue. A curettage yielded abundant soft tissue, grayish-pink in color, interspersed with a generous amount of freshly coagulated blood.

Microscopic examination of the curettings showed a thick endometrium, markedly spongy in appearance, due to the presence of numerous dilated, irregularly shaped glands lined by a secretory epithelium of the lutein phase. The interglandular stroma was edematous, hemorrhagic, and showed a diffuse infiltration by decidual cells. Necrobiotic changes were present in places and, in these areas, numerous granulocytic cells and thrombosed blood vessels were present. Elsewhere chorionic villi were recognizable. Some showed advanced retrogressive changes, while others were still well preserved and displayed pluristratification, in irregular fashion, of trophoblastic cells. Among the latter, cells with characteristics of Langhans' cells prevailed and only a few syncytial cells were noticeable here and there. The striking finding, however, was that of large, oddly shaped, deeply stained cells which did not resemble either the Langhans' or the syncytial or the decidual cells. These large cells showed great variations in size and shape, nuclear giantism, at times two or three nuclei, but, even in the thinnest microscopic section, due to pronounced hyperchromatism, no nuclear details could be made out, and, as the cytoplasm also was deeply stained, the limits between nucleus and cytoplasm could not be seen distinctly. Cells, identical in type, either scattered or in clumps, were found also at a distance from the chorionic villi, in the interglandular endometrial stroma, and in fragments of myometrial tissue obtained at curettage. (Fig. 3.) As the cells penetrated in between the muscular fibers, they showed a tendency to assume an elongated or spindled shape and to fuse together with loss of boundaries and of cellular outlines. (Fig. 4.) This resulted in the formation of plasmodial masses which appeared to be most numerous in the proximity of thin-walled blood vessels. No actual invasion of blood vessels could, however, be detected and mitotic figures were never seen among the proliferated cells.

In this case also, the impression was an atypical trophoblastic cells proliferation, perhaps less severe than in the previous case, and fitting in the category of the so-called syncytial endometritis. The course of the process was closely followed with frequent gonadotropic hormone tests. After two months they were still negative, and after a nine-month interval the patient is in excellent health.

Comment

If the criteria usually advocated in the differentiation between a hyperplastic or a displastic cellular growth elsewhere in the body had been applied to the patterns observed in the two cases under consideration, the final judgment might have been that of a malignant process, and the process treated accordingly; but it has been already known that the criteria of malignancy in the cellular growths elsewhere in the body do not apply directly to this particular type of uterine growth. In the discussion of Hertig and Sheldon's paper, this point has been stressed by Novak.[15] Since invasiveness, with consequent obliteration of neighboring structures, is a quality inherent to the trophoblast under normal conditions, it is obvious that we must turn our effort to the detection of other criteria in trying to evaluate the nature of the process.

Amount and depth of the cellular infiltration of course are important, but obviously cannot be considered the decisive criterion, since deep penetration of trophoblastic cells in the uterine wall is said to occur in the normal pregnant uterus.

More valid information, in our opinion, can be obtained by the careful study of the cytologic characteristics of the cell type mainly involved in the proliferative process. In our two cases, as in the cases of others, variously

interpreted as atypical chorionepithelioma or syncytial endometritis or syncytioma, the role of the invader was played mainly by large, round, polyhedral or bizarre-shaped cells with hyperchromatic nuclei and slightly acidophilic cytoplasm. These cells showed a tendency to enlarge to gigantic proportions, the enlargement being due mostly to swelling of the nuclei; and, as the cells enlarged, the nuclei became further hyperchromatic and displayed evidence of karyorrhexis and karyolysis, signs of impending cell dissolution. Mitotic figures were not seen in our two cases and very rarely were mentioned in the description of similar cases by others.

A number of terms, such as wandering cells, chorionic wandering cells, chorioectodermal syncytial wandering cells, syncytioblasts, puerperal cells, unknown cells, have been proposed for these types of cells, which older writers regarded as decidual cells, and which most of the modern authors consider of fetal origin. The different names proposed are indicative of the lack of agreement among the authors on the nature and significance of these cells. Among the terms proposed, "syncytial" has been accepted, due to the strong resemblance of these cells to the syncytial cells of the epithelial covering of the villi. Schmauch[6] and Greenblatt and Pund[12] found them to resemble decidual cells. We often received the same impression but one cannot judge on pure resemblances. According to Schmauch,[6] these cells do not originate from the syncytial cells, but from the "finest sprouts" of the Langhans' cells, which have undergone a plasmodial change. Greenblatt and Pund[12] have coined the term "metasyncytium" for these "plasmodial ribbon-like masses" which, in their opinion, are derived from and appear to be a later stage of Langhans' cells.

Regardless of the discrepancies that still exist as to the origin of these cells, all authors agree that the "plasmodial pattern" represents a form of reduced vitality of the trophoblast. Ewing[7] has made this clear when he first employed the term of syncytial endometritis to replace Marchand's atypical chorionepithelioma. The presence of cells of identical character in regressing hydatid moles, degenerating choriomata, destructive moles, placentary polyps, and around necrotic villi is further evidence of the retrogressive character of these plasmodial masses, for which it might be proper to speak of "hypertrophic degenerated trophoblastic cells." Rosenzweig[9] also is against the neoplastic nature of these cellular structures, and the same opinion is advanced by Greenblatt and Pund[12] and by Choisser and Notes.[13] A number of reports in the literature claiming spontaneous recovery of choriomatous growths seem to justify Ewing's contention that the trophoblastic cells can carry aggressive tendencies for a while, then lose their developing power, and finally undergo a process of reduction.

While the harmless nature of our two cases is clear, it is difficult to explain the stormy proliferation and invasion by trophoblastic cells which preceded their regression. Loss of "restraining factor" might be an explanation, but, in our opinion, the existence of a "syncytiolysin" is not demonstrated convincingly enough. Hormonal dysfunction is another possibility, but again we are in the field of the hypothesis, difficult to prove. Necrobiotic hemorrhagic changes, thrombosis of blood vessels, and diffuse infiltration by inflammatory cells were outstanding findings in both our cases, and they have been emphasized

in a number of similar cases reported in the literature. Perhaps local disturbances in blood flow and nutrition led to persistence and excessive production of trophoblastic cells, to their drawing down into the uterine muscle, and, finally, to their decadence, through a series of retrogressive changes.

It is generally agreed that biologic hormone studies are of very definite value in estimating trophoblastic activity. Since elaboration of the chorionic hormone is a property inherent in the chorionic tissue, demonstrable quantities of hormone are expected to be found in the body fluids of any person harboring such tissue, either normal or abnormal. As far as we know, this expectation has never failed yet, despite the few published reports of misleading results, which threw a justified doubt on the real value of the method. Greenblatt and Pund[12] have mentioned the case of Schumann and Voegemin in which the histologic diagnosis was inconclusive after two curettings and, because of two negative Freidman tests, operation was delayed. Four months later the patient had a massive hemorrhage; the Freidman test was at this time strongly positive and a hysterectomy was performed. On histologic examination, a typical chorionepithelioma was found, and the patient died five months later of cerebral metastasis. If our understanding of the histobiology of these tumors is correct, no explanation can be offered to justify the early negative chorionic gonadotropin assay (in this case) except possibly unfitted animals or errors in specimens or technique.

Against the conclusive value of the method, Brindeau[16] has stressed the point that because of the prolonged period of hormone elimination, the persistence of a positive assay, after expulsion of the mole, does not necessarily indicate that a malignant change has occurred in the molar rests. This statement was based on Zondek's[17] demonstration that the pregnancy test may remain positive from four to twelve weeks after elimination of the mole. Under these circumstances, if qualitative positive tests may be viewed with suspicion, spaced hormone titration of the blood serum has been shown to permit differentiation between persistence of physiological condition and development of a pathological one. As Payne[18] has pointed out in the discussion of Hertig and Sheldon's paper "the only hormonologic identification of chorionic malignancy rests, not upon a single quantitative or qualitative determination, but upon the demonstration of increased values by means of repeated assays."

One might conclude that an effective distinction between the malignant trophoblastic cell growths, which require radical treatment, and the harmless trophoblastic cell proliferation for which such treatment would represent an undesirable mutilation must be based in each case upon careful consideration of the clinical, pathologic, and hormonic data.

Summary and Conclusions

Disorderly, atypical, overactive trophoblastic cell proliferation and myometrial invasion by large bizarre-shaped cells which showed a marked tendency to fuse together in plasmodial-like formations were the main histologic patterns found at examination of deep uterine scrapings in two cases following miscarriage. In one case, that of a 22-year-old white woman, pregnancy had advanced up to the second month; in the other, that of a 19-year-old white woman,

pregnancy had advanced up to the fourth month. Following the study of the microscopic slides, the impression received was of a so-called syncytioma in the first case and of syncytial endometritis in the other case. Radical treatment was considered in both, but delayed in view of the youth of the patients and of some doubt as to the real malignancy of the condition. The process was followed through frequent gonadotropic hormone tests and repeated curetting. The hormone tests were consistently negative in both cases. In the first case, a curettage after a month revealed a perfectly normal endometrium in the secretory stage of the menstrual cycle. There were no detectable trophoblastic cells in the fragments of myometrial tissue.

In the light of the unusual course of events in these two cases, and in similar cases reported in the literature, it is apparent that the usual criteria of malignancy, which apply so well to the cellular growths elsewhere in the body, cannot be applied strictly to the growths by trophoblastic cells, since free cellular growth, invasiveness, and obliteration of neighboring structures are qualities of the trophoblast under normal conditions.

In the differential diagnosis between benign trophoblastic cell proliferation and chorionepithelioma, it is felt that valid information can be obtained from the intimate structure of the cell type mainly involved in the proliferative process. On the basis of cytologic criteria, namely, absence of mitotic figures, evidence of impending cell dissolution (nuclear hyperchromatism, karyorrhexis, karyolysis) and predominance of "plasmodial patterns" which more and more are considered to represent a form of reduced vitality of the trophoblast, in spite of the cellular atypism and of the deep invasion of trophoblastic cells in the uterine musculature, we decided to treat our cases expectantly. The final outcome proved our judgment to be correct.

References

1. Marchand, F.: Monatschr. f. Geb. u. Gyn. **1**: 419, 1895; Ztschr. f. Geb. u. Gyn. **32**: 405, 1895; Ztschr. f. Geb. u. Gyn. **39**: 173, 1895; J. Obst. & Gynaec. Brit. Emp. **4**: 74, 1903.
2. Schmorl: Quoted by Ewing, J.[7]
3. Frankl, O.: Handbuch d. Frauenheilkunde, Liepmann, Leipzig **2**: 136, 1914.
4. Ruge, C.: Quoted by Schmauch.[6]
5. Velits, V.: Ztschr. f. Geb. u. Gyn. **52**: 301, 1904.
6. Schmauch, G.: Surg., Gynec. & Obst. **5**: 301, 1904.
7. Ewing, J.: Surg., Gynec. & Obst. **10**: 366, 1910.
8. Vineberg, H. N.: Surg., Gynec. & Obst. **28**: 123, 1919; J. Mt. Sinai Hosp. **10**: 12, 1943.
9. Rosenzweig, M.: Am. J. Obst. & Gynec. **13**: 563, 1927.
10. Ferguson, J. H.: Tr. Edinb. Obst. Soc. **44**: 212, 1923-1924.
11. Geist, S. H.: Surg., Gynec. & Obst. **32**: 427, 1921.
12. Greenblatt, R. B., and Pund, E. R.: South. M. J. **31**: 140, 1938.
13. Choisser, R. M., and Notes, B.: J. A. M. A. **109**: 1628, 1937.
14. Hertig, A. T., and Sheldon, W. H.: Am. J. Obst. & Gynec. **53**: 1, 1947.
15. Novak, Emil: In the Discussion of Hertig and Sheldon paper.[14]
16. Brindeau, A.: Presse Medicale **43**: 1017, 1935.
17. Zondek, B.: J. A. M. A. **108**: 607, 1937.
18. Payne, F. L.: In the discussion of Hertig and Sheldon paper.[14]

EARLY RISING AFTER DELIVERY*

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EARLY ambulation in the puerperium is taking on increasing interest to the obstetrician and later it will probably occupy attention of the gynecologist.

During the recent war the shifting population made some centers so crowded that hospital facilities could not keep up with the demand. Therefore, physicians and administrators were forced to attempt to admit more patients per bed than was customary. They could do so only by allowing surgical and obstetric patients up earlier, thus hoping to discharge them sooner. Lack of hospital personnel also entered into the problem.

In Chicago after the war, the demand for obstetric care has risen about 100 per cent or more, yet we have no more obstetric beds and bassinets available. Most women do not wish to have their babies at home. The hospitals and the medical staffs have been forced, by demand and by lack of personnel, to shorten the stay of obstetric patients wherever possible.

In Chicago, patients are permitted to stay in the hospital from three days to seven or eight days. The 3-day patients are usually sent home in an ambulance, while those staying five or more days are permitted to leave by private car or taxicab.

Approximately a decade ago, the first attempts at early ambulation following major surgical procedures were instituted. Although varying interpretations have been placed on the results, the procedure seems to be basically sound.

The question of when to allow the patient to get out of bed, for how long a period, and exactly how much freedom of movement is permitted is a point for the physician managing the case to decide.

About eighteen months ago, the Henrotin Hospital was faced with the problem of delivering and housing twice as many patients, with short personnel. The obstetric staff decided it was better to offer at least delivery service and fewer days in the hospital. Previous to this time, the hospital followed the usual generally accepted routine in this community. The patient was allowed to sit up in bed on day 4, to dangle the legs on day 7, up in a chair on day 8, to walk on day 9, and to go home on day 10 to 12.

It was decided to attempt to get all patients on their feet on the fourth day with the exception of those who might have developed complications. For the purpose of clarification, the postpartum day is defined in relation to 6:00 P.M. Those mothers who are delivered prior to 6:00 P.M. commence their second postpartum day at midnight of the same day. Those delivering between 6:00 P.M. and 12:00 midnight commence their first postpartum day at midnight.

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On the morning of the fourth day the patient is given an enema and is then encouraged to use the toilet unaided, but accompanied by the nurse. From the toilet the patient returns to a bedside chair where she is allowed to remain for fifteen to thirty minutes, or until the bed linen is changed. The patient is allowed up to the toilet whenever necessary during that day and also to remain seated for fifteen to twenty-minute periods immediately thereafter. The same procedure is followed on the fifth day with the addition of some walking about the room. From the fourth day on, the patient is encouraged to perform as much of her daily ablutions as possible. A basin of warm water, soap, washcloth and towels are brought to each bedside table.

On the sixth day the patient is allowed to walk around the corridors and to the nursery. On the seventh day she takes a shower and is given complete freedom of action and movement. This continues as long as she remains in the hospital.

The average hospital stay at present is seven days; the number of hospital days is directly related to the number of nursing personnel available.

In following this routine one can expect to meet with objection on the part of some of the patients. Those who have just been delivered of their second, third, or fourth child will many times express amazement at the procedure and in some cases they will be antagonistic. There are various methods to cope with this situation. When the patient refuses to get up at the nurse's bidding, the intern or resident is called to add his encouragement. In the event that this meets with failure, the attending physician is appraised of the facts prior to making his daily rounds. Many times the answer is only to allow the patient another day in bed, and in approximately 5 per cent of this series two extra days were allowed.

Reasons for objecting to arising on a given day are many and varied. The patient who assumes an air of martyrdom will always be present. She has passed through the tortures of labor and is not ready to reveal an uneventful postpartum period by being out of bed.

The observations upon which this present study is made are based on 1,000 deliveries at Henrotin Hospital, representing a typical cross section of postpartum cases. Included in the group are 53 low cervical cesarean sections. Of these, twenty-eight were up to the toilet and sitting in a chair on the first postoperative day, seven on day 2, one on day 3, three on day 4, seven on day 5, seven on day 6. The first postoperative day is defined as the day following surgery.

Of those patients delivered vaginally who were up on day three and four, the following observations have been made:

The first day that the patient is up we recognize an attitude of scepticism or possibly an air of anticipation. She asks herself, "Just how am I going to get along today? What is going to happen?" The patient moves with an air of hesitancy and with varying degrees of discomfort, for many have had an episiotomy. There is a tendency to return to bed in a very short time.

On the second day up the patient has much more assurance of her ability to ambulate. She moves about with freedom of effort. There is an air of confidence reflected in her movement and, in a large percentage of patients, an attitude of a job well done. There are others, however, with a normal degree of emotional stability who retain some doubt as to the advisability of being out of bed. Their remarks are in the nature of the statement that "everything inside me feels as though it is falling out." This thought is expressed equally by the primipara as well as the multipara.

On the sixth postpartum day the patient is effortlessly walking about her ward or room and the corridors. She is inclined to make frequent trips to the nursery to view through the windows her own and other infants. The opportun-

TABLE I. DAY UP

	1	2	3	4	5	6	
Primiparas		3	120	221	52	16	412
Cesarean section	12	4	0	2	4	6	28
Multiparas	1	2	135	287	76	34	535
Cesarean section	16	3	0	1	4	1	25
Total							1,000
Per cent	2.9	1.2	25.5	51.1	13.6	5.7	100

TABLE II. DAY HOME

	5	6	7	8	9	10	11	12	13	14	15	16	17	
Primiparas	13	61	90	112	70	41	13	8	1	1		1	1	412
Cesarean section			1	5	8	6	4	2	1	1				28
Multiparas	20	74	102	148	96	76	9	8			0		2	535
Cesarean section				6	6	8	5							25
Total									1					1,000
Per cent	3.3	13.5	19.3	27.1	18.0	13.1	3.1	1.8	.02	.02		.01	.03	100

TABLE III. TYPE OF DELIVERY

	PRIMIPARA	MULTIPARA
Cephalic forceps	352	300
spont.	39	223
Breech forceps	9	2
spont.	12	16
Low cervical cesarean section	28	25
Version & extraction	0	1
Episiotomy	376	370
Total Babies	1007	

ity to observe her child is a source of pleasure to the new mother. From this point on to the time of discharge the routine is unchanged.

At the time of discharge the patient walks confidently and effortlessly out of the hospital. It would be difficult from ordinary observation to classify the individual as a recent parturient. During the period of hospitalization the patient is given the same close observation that has been the rule in the past. With any evidence of complications she is returned to bed rest or to limited movement.

No attempt has been made to run a control group against this series as it is felt that the reaction of the average patient during the customary postpartum period has been definitely established.

TABLE IV. COMPLICATIONS

	PRIMIPARA	MULTIPARA
Episiotomy	Partial separation Up day 4 Home day 12 2nd repair Up day 3 Home day 16	Partial separation Up day 4 Home day 10 Partial separation Up day 4 Home day 11 2nd repair Up day 4 Home day 17
Mastitis	Up day 3 Home day 9 4 11 4 12 5 12 5 14 6 9	None
Urinary tract infection	Up day 4 Home day 9 4 10 4 11	Up day 4 Home day 11 5 9
Mild upper respiratory infection	Up day 4 Home day 8 4 9 5 10 5 10	Up day 3 Home day 6 4 9
Fever unknown origin	Up day 3 Home day 11 3 17	Up day 4 Home day 9
Endometritis	None	Up day 5 Home day 17
Vertigo and syncope	None	Up day 6 Home day 10 4 8
Hemorrhage	None	Mod. severe Up day 5 Home day 12 Mod. severe Up day 5 Home day 10

In this series there were five patients who suffered various degrees of wound breakdown in the episiotomy. Two were considered extensive enough to require a return to surgery. In each case figure-of-eight silkworm-gut sutures were used for the secondary repair. The remaining three were allowed to heal by granulation. In each case there was some elevation of temperature, with two patients reaching 100.4° F. on two or more days.

Vertigo is not an infrequent symptom but rarely occurs after the first day up. This complaint was not unusual in many who remained in bed under the previous routine of eight or more days.

Vertigo was followed in two cases by syncope. In the first case no explanation could be found. In the second, there was a strong psychic factor which probably contributed largely to this episode. The patient was returned to bed and she was up again on the fifth day without incident.

In none of this series was there detected a case of thrombophlebitis while in the hospital. One patient, a low cervical cesarean section case, who was up on day 7 and discharged on day 12, returned to the hospital with severe thrombophlebitis, eighteen days following discharge from the hospital.

The incidence of proved cystitis was at a minimum, three cases being established by clinical and laboratory methods. *E. coli* was the predominant organism found on culture of the urine.

Mastitis of varying severity from mild to severe was present but it is not probable that this could justly be attributed to earlier rising.

Fever of unknown origin is a factor that will persist. This classification is given only to those patients in whom a thorough study of all genital and extragenital sources reveals no apparent reason for an elevation in temperature over 100.4° F. for one or more days. The patient returns to bed and remains until the temperature remains normal for twenty-four hours.

It is felt that normal bowel habits are more quickly reestablished with early ambulation. The necessity of catheterization is also reduced. The uterus returns to normal size more rapidly.

There are frequent occasions when it has been found necessary to discharge the patient on day 6 and many times on day 5. The procedure is unchanged irrespective of the day of discharge. The patient in every case left the hospital ambulatory, although we do not attempt to condone or to establish early discharge as a practice, but do this only because of overcrowding. Prior to discharge the patient is instructed to follow a restricted routine at home, one that would correspond to her movement if she remained in the hospital for ten or twelve days.

All the staff at Henrotin Hospital state they find no greater pathology at the postnatal examination than they did when the patients remained in bed eight days or so.

Whether or not early rising will have late aftereffects such as relaxed abdominal muscles, relaxed pelvic floor, prolapse of the uterus, bladder and rectum remains for the future to determine. Most obstetricians have felt that bed rest of a week or more was necessary for the proper return of the pelvic organs to normal. Thirty years ago it was customary to keep patients in bed twelve to fourteen days. Most women then did not fully return to their predelivery state under six weeks. With earlier rising, most women today feel as well as they did before delivery in about fourteen days. Perhaps this is better, but who knows? Will our American women be as good looking at 45 years, or will they look old at 35, like the Indian women in Central and South America where they resume their usual routine in twenty-four to forty-eight hours?

Conclusions

One thousand patients were allowed up on day 6 or earlier with 80 per cent of these being up prior to day 5. These patients are apparently in much better condition at the time of discharge than if they had remained in bed for eight or more days. They are in a position to adapt themselves more readily to their daily household routine. Episiotomy wound healing was not adversely affected nor was morbidity increased.

No case of thrombophlebitis occurred in those delivered vaginally, which causes us to believe the tendency toward this complication is reduced.

No case of uterine prolapse occurred. The rate of involution of the uterus is increased.

When necessary, because of overcrowding, the patient may be discharged from the hospital earlier than heretofore with a greater margin of safety.

The postoperative course of the cesarean section cases is more nearly uneventful. Distention is infrequent. The necessity for catheterization and enemas is lessened when the patient is up to the toilet on postoperative day one. One case of thrombophlebitis occurred thirty days post operation.

References

Blach, B. W.: Mod. Hosp. 60: 52-53, 1943.
Rotstein, M. L.: J. A. M. A. 13: 838-840, 1944.

Discussion

DR. ALFRED J. KOBAK.—The wide range of possibilities as reported in this paper does not indicate to what extent the authors themselves allow their own patients out of bed following vaginal deliveries and following cesarean section. Emil Ries was probably the father of early ambulation; about forty-eight years ago he wrote a paper which appeared in the Journal of the American Medical Association on this subject. His colleagues were reluctant to accept his views. He was far ahead of his period and consequently his suggestions were ignored. From time to time afterward, there appeared contributions by general surgeons which indicated the possibility of early ambulation. In the past twenty years there has been a recognition of early ambulation, and latterly patients delivered vaginally have been given attention in this same respect by permitting them out of bed early. Recently a volume appeared by a surgeon in which the physiologic principles of early ambulation were discussed. The author contends that there are fewer pulmonary and circulatory complications with consequent thrombosis and emboli, less abdominal distention, and less wound complication.

In the literature we find reports of animal experimentation in which dogs and rats were subjected to early ambulation and in the control animals early ambulation was avoided. It was found that the animals that rose early had far better recovery.

We began our studies on obstetric early ambulation in the early part of 1940 at the Cook County Hospital. We were inspired by the reports in the magazines of the air blitz over London where patients were removed from their beds. We had no known principles to guide us, but we let the patients up on the fifth, then the fourth, third, and second days. We studied 500 such cases and we were entirely satisfied that these patients had better results in convalescence when compared with the control group. We were prompted to try another 500 but because of the shortage of nurses the study was not completed. We recently resumed this study. In Ward 51 of the Cook County Hospital we house patients who have a normal uneventful pregnancy and these patients we ambulated on the second day. There were 1,417 with a corrected morbidity of 1.7 per cent. In the control cases that were up on the fifth and sixth days there were 847 and the morbidity was 2.8 per cent.

A study of three months' duration was conducted on patients in Ward 50 which houses those with septic complications. These were allowed up on the sixth day. There were 123 with a morbidity of 2.66 per cent and 84 with a morbidity of 4.55 per cent. These patients had a morbidity 1.7 times higher than the early-ambulated cases.

Concerning cesarean section, for three months we had 33 cases permitted out of bed as compared with a control group of similar size. The average postoperative stay was nine days as compared to 13 days in the control group. The morbidity incidence was 6 per cent as compared to 10 per cent. There were more inhalation anesthetics in the control group and more spinals and locals in the group studied.

In asking the nurses concerning the progress of the people ambulated early, they reported it was entirely satisfactory but they did observe that the lochia was more profuse on the first day, but the day after it decreased. Involution occurred rapidly. There was less necessity for use of the bedpan; most patients would prefer to go to the toilet and eliminate the uncomfortable posture of using a pan in bed.

I feel the authors did not get full benefits of early ambulation, that their ambulation was resorted to rather late. We have ambulated our patients much earlier. It was shown in the book referred to that cases that were ambulated soon after anesthesia, on the first and second day, did much better. He quotes the work of de Takats and others showing that trauma at the time of surgery gives rise to changes in the blood that cause the blood to coagulate more rapidly. This together with the fact that the patient is immobilized are factors which lead to thrombosis. If thrombosis can be prevented it has to be prevented by early ambulation.

DR. GARWOOD C. RICHARDSON.—The authors have recommended early ambulation apparently as a relief for the crowded situation in many of our hospitals in Chicago and throughout the country. Those of us who practice early ambulation at Wesley Hospital do so for the virtues of the procedure itself; in other words, for the benefits we feel the patients derive from early ambulation. During my internship days at the Ancon Hospital in the Canal Zone, in 1921-1922, patients were gotten out of bed on the first postoperative day after major surgery. Certainly the literature cites many articles in surgery and in obstetrics where early ambulation has been practiced. In their opening statement the authors say that it will probably be extended to gynecology. By certain doctors early ambulation in gynecology has been practiced in Wesley Hospital as long as early ambulation has been practiced in obstetrics.

According to the authors, the sixth day is apparently the accepted criteria for early ambulation. We feel that early ambulation should not be extended over a three-day period. If you really are practicing early ambulation for the sake of early ambulation, the patient should be gotten up on the first or second day and certainly by the third day. At Wesley Hospital since early ambulation was instituted we have had 4,101 deliveries. Our attending men there are divided into three groups: Those of us who get our patients up from the first to the third day compose the first group, and the number of those cases amounted to 1,247. The second group are probably just a little hesitant—they constitute some of the younger men—and they get their patients out of bed in four or five days. The number there was 174. The third group constitutes those men who get their patients up from the fifth to the sixth day. That is probably due to the policy that we have adopted of not requiring anyone to go home earlier than eight days. The number in this group was 394, making a total within the six-day period of 1,115 cases.

We believe that the patient is definitely benefited by early ambulation. We have tabulated the observations of attending men, nurses, interns, and residents. There are about eleven benefits that we see are derived from early ambulation.

1. Voiding is more spontaneous, with a definite decrease in the number of cases that have to be catheterized.

2. Defecation normally is earlier than usual. We do not use enemas except where necessary in those cases that are allowed up early.

3. The perineal comfort of the patient is definitely benefited. Early ambulation and proper exercise of the muscles in the region of the episiotomy wound cause much more rapid recovery.

4. Fainting has been practically eliminated. Many patients faint when gotten up on the eighth day; practically none faint when they are gotten up on the first to the third day.

5. Involution is aided. That is an observation that even student nurses have noted quite commonly. By the time the patient goes home you can very frequently not feel the uterus abdominally.

6. Total hemorrhage is lessened.

7. The patient is happier, we find, rather than skeptical. That could be due to the fact that we do not just give her a surprise when she is in the hospital by telling her we are going to get her up early, but include that as part of her prenatal care. All my patients are informed during their prenatal care that they are to be gotten out of bed on the first to the third day, depending on their condition. In my own cases I have had only two complaints, and these two individuals refused to get up early.

8. Thrombophlebitis is lessened. Embolism has been cited in the literature as being lessened. In the studies presented this evening the period has not been long enough to bring out the possibility of lessened frequency of embolism.

9. We are reporting less morbidity than formerly.

10. The patients practices self-care earlier in her hospital stay and thus reduces the burden upon the nursing staff.

11. We have had no cases of complete disruption of the episiotomy repair.

In the tabulation of cases as presented by the authors, they show a total of 1,000 cases over a six-day period; 511 of those were gotten up on the fourth day and only 296 were allowed up in the first three days. That is only about 30 per cent that really qualify as what we would consider truly representative of early ambulation. In the portion of the table that was accompanied by complications, there were 55 cases representing 74 patient-days where the stay was beyond ten days, clear up to as long as 16 days in one case and 17 days in another case. It is not clear from the tabulation whether those were early ambulation cases or what the complication was. It does seem that that number of patients and that number of patient-days are a little bit excessive in a report presenting 1,000 cases.

DR. JOHN BREWER.—At St. Luke's Hospital for many years we have been getting our patients up between eighteen and thirty-six hours postoperative. That includes all gynecologic procedure, vaginal and abdominal.

DR. C. O. McCORMICK, Indianapolis, Ind.—At our hospital it has been our impression that we had fewer residual complaints and fewer emboli when we practiced early ambulation.

I would like to ask regarding circumcising the babies. Is it done immediately or are the patients allowed to go home and later return for this procedure?

DR. J. P. GREENHILL.—I would like to emphasize one important aspect of the subject. Those of you who read the Year Book know that I am in favor of early ambulation. I learned it from Emil Ries. His paper in 1899 was the first one in this country on this subject and the next one was by Howard Kelly of Baltimore in 1911.

There is a definite connection between lying in bed and the incidence of thrombosis and embolism, both fatal and nonfatal. Erdheim of Vienna taught his classes that the source of his emboli, both fatal and nonfatal, was in the calf vessels. To try to dissect out every vessel in the calf was an enormous task. He cut clear across the calf and found, to his amazement, that while there was the preparation of a thrombus in the veins there was no evidence of thrombosis. In the last few years a number of investigators in this country and abroad followed up that study, and in one series there were 26 per cent of thrombi and in another series 50 per cent. In one group in which there was a series of fatal emboli, every single death occurred in patients who had been in bed from the time of the operation to death. Not a single embolus was found in patients who had been up shortly after surgery. In these studies, if early ambulation was not possible, then they made the patient move about in bed. I think the older men and some of the younger who are still skeptical should read these papers.

DR. ROBERT M. GRIER.—At Evanston Hospital we get our patients up early. As to morbidity with special reference to breast abscess, I think the morbidity would be greatly lessened if we sent the patients home on the first day.

DR. W. J. DIECKMANN.—For over fifty years there have been enthusiastic reports every ten to fifteen years about early ambulation. The reports are always favorable but soon most hospitals discontinue early ambulation without reporting the reason. If it is so wonderful, why has it been given up in the past? I do not like the term "getting on the band wagon," concerning early ambulation for obstetric patients. I do not know if it is good or bad for the patient. As the result of studies on puerperal infection in 1925, I have always believed in early activity of the patient in bed. Whether or not she has to be up is still debatable. I am certainly opposed to the discharge on the third, fifth, or seventh day post partum. I do not believe any hospital is justified in this procedure. When beds became scarce, the hospital authorities and city authorities should have cooperated and made beds

available. Much of the elective surgery, gynecologic and general, could have been omitted during the emergency. I do not believe the doctor should have assumed the responsibility for taking care of the increased obstetric load by merely discharging patients at earlier dates.

When one considers early ambulation, there are several questions; (1) Is it good for the patient in that complications are decreased, and are her general morale and strength better two weeks after delivery than they would be were she kept in bed the usual length of time? (2) Does it decrease the amount of nursing care and thereby reduce hospital costs? I am quite certain that there will be a scarcity of nurses for a long time and, if nurses are paid what they deserve, hospital costs will increase instead of decrease. They are already very high for the family with the average income. If the costs of hospital care can be decreased without endangering the patient, it is worth while.

I am opposed to patients being discharged before the tenth day, which I think is too early, and would prefer the fourteenth day, the reason being that once the mother is home she is concerned with the general management of the house, irrespective of how many servants there may be. There is less or no control of visitors possible. There are disadvantages in the hospital, but I believe that those at home outweigh those in the hospital.

For economic reasons we began over twelve years ago to have our obstetric patients bathe themselves on the second postpartum day. This has continued to date and we have believed for some years that this early activity in bed is of value. The sick patients, of course, have complete nursing care. On October 1, we began letting a limited number of patients up earlier in the puerperium. The doctors and nurses were pleased with this trial period. Since January 1, all obstetric patients including cesarean section cases are out of bed in a chair twenty-four hours after delivery, and forty-eight hours after delivery are permitted in the bathroom which adjoins their bedroom and by the sixth day after delivery are permitted in the corridors of the hospital. The only patients who do not get up are patients from whom it is necessary to obtain the urine by a retention catheter, for instance, toxemic patients, or patients who have had major complications. All the doctors on the staff are cooperating in this endeavor. To date there have been no increased number of complications and the nursing staff states that the amount of nursing care has been decreased tremendously. No patient is compelled to get up, and patients are discharged on the tenth day, or, if the bed is not necessary, are permitted to stay longer.

We expect to compare our statistics at end of this year with those of preceding years and from a comparison of that data decide whether or not we will continue early ambulation.

Early ambulation in our hospital was not instituted to enable us to increase the number of deliveries or to facilitate the early discharge of patients. We insist upon patients staying the prescribed number of days, which is a minimum of ten.

DR. FREDERICK H. FALLS.—We heard it stated here that Emil Ries said it was a good thing to take patients out of bed. If you had talked to John B. Murphy he would have said it was not a good thing. E. Wyllys Andrews would have said it was not a good thing. If you asked Graves at Harvard he would have said, you had better keep a perineorrhaphy case in bed for sixteen or seventeen days and you will get better results. This idea of getting all excited about a situation that is present with us at this time is ill advised. It has been precipitated by this war condition and somewhat by spinal anesthesia. The reason for this wave of spinal anesthesia was because the Army and Navy did not have anesthetists and they could not get them, so they stuck a needle in the back of the patients and operated upon them without a proper type of anesthesia.

If you know anything at all about labor, and especially the second and third stages, and if you ever put your hand in the vagina and felt a flaccid ureterosacral ligament and perineum, it seems to me you will agree that to put the weight of a puerperal uterus on this ligament the first, second or, third day is ill advised if you do not have to do it. It does not make any difference whether these women leave the hospital without fainting, that does not mean anything. Maybe they do feel better and maybe they are stronger on their feet, but that does not tell what is going to happen to those women in ten or fifteen years. The

only way to settle it is to take every other case—and you have to take enough of them, 1,000 or 5,000 to find out and then you will begin to see the difference. I do not believe we will know whether the women who have been allowed to be up are better off than those who were kept in bed longer for another ten or fifteen years. Then we will know whether somebody has done them a favor or an irreparable wrong.

DR. CORNELL (Closing).—Some of the men misread the title. It was "early rising after delivery," not after gynecologic operations. The statement was made that the gynecologist would be interested in these patients at a later date. It had nothing to do with early rising in gynecology.

The second thing is that we have a similar situation to that which Dr. Richardson has at Wesley. Most of our patients are private patients. It is, as you know, rather difficult to get physicians to agree, even in a more or less closed staff. We have some doctors who wish to have their patients up on the third day, some on the sixth, and some on the eighth day. It is only recently that some of the men have come around to earlier rising. That is the reason you see the figures that were mentioned in these 1,000 cases. In the past six months most of the men operating at Henrotin Hospital permit their patients to get up on the third day and they are discharged on the fifth to the seventh day if there are no complications. The ones that were in the hospital sixteen and seventeen days were patients that had secondary repair of episiotomies. Aside from that, there were none of the early rising patients who stayed longer than ten days with the exception of a few who had had cesarean sections.

About six months ago I started to get the patients who had cesarean section up early. I had a considerable amount of difficulty with the patients themselves. It was only by moral persuasion and getting the patient out of bed myself that I was able to get them to sit in a chair the second day. The distention is practically nil, we have fewer catheterizations and the uterus seems to involute better. I am not sure whether it is good policy or not. As you probably all know, I was brought up by Dr. DeLee, who definitely advocated, when I was first with him, twelve days in bed. It took several years before he permitted a patient to get up in ten days and finally in nine days. I do not think he would advocate getting them up on the first, second, or third day. I do not believe I am going to live to see the patients I deliver now come back with gynecologic problems, the result of early ambulation. Whether or not they are going to have relaxed perineums for the gynecologist to repair, prolapses and other things, it is difficult to say. I have a feeling that some of the younger men will see these patients. I just wonder whether it is good policy. I have a feeling that it would be wise for us to go back and keep these patients in bed a little longer and keep them in the hospital a little longer. I have seen Indian women in Central America and Guatemala who get up twenty-four hours after delivery, but these women look old at 30 or 35 years.

In answer to Dr. McCormick's question, the babies return later for circumcision.

It seems to me that the number of cases of mastitis is somewhat lessened, though 1,000 cases do not mean anything. I just want to leave the thought with you that I do not believe we are doing our patients any good by permitting them to get up as early as possible and to allow them to go home as early as possible.

ACUTE PUERPERAL MASTITIS

Clinical and Bacteriologic Studies in Relation to Penicillin Therapy*†

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ACUTE mastitis is a serious medical and psychological complication of the puerperium, especially if suppuration occurs. It is serious medically: first, because it may be extensive and destructive and may endanger life; second, because it may be associated with multiple or chronic recurring abscesses, thus having a deleterious effect upon health; and third, because it interferes with proper lactation and almost always necessitates the discontinuance of breast nursing. Acute mastitis is serious psychologically because it disrupts the home and necessitates hospitalization; because the patient becomes anxious about further complications incidental to her puerperium; and because of fear of a similar experience in any subsequent lactation. Irrespective of the time of the development of mastitis, the patient is not psychologically prepared for this complication.

Among our patients, mastitis has been most often observed within the first eight weeks of the puerperium, usually after the tenth day. However, observations beyond the third month have been limited, due to the small number of mothers continuing breast feeding after this time.

The early treatment of acute mastitis may often bring about subsidence without suppuration. On the other hand, virulence of the infection, lowered host resistance, or delayed treatment may explain unfavorable results. Prior to the use of penicillin, the only effective but seldom employed method for treatment was the immediate drying of the breasts after delivery. Ordinarily such a routine would seem too great a price to pay. The report of Hodgkinson and Nelson[1] on 24 patients with acute puerperal mastitis who were spared suppuration by the use of penicillin seemed to give the impression that suppurative puerperal mastitis could be completely avoided by the use of penicillin therapy. Using the same treatment, Power and Cravotta[2] obtained cures within forty-eight hours in 25 cases of acute mastitis. Hence, penicillin was acclaimed a panacea for human mastitis.

Somewhat different results observed at the Chicago Lying-in Hospital have stimulated the present report. This study includes observations on 210 patients with suppurative mastitis seen during the last thirteen and one-half

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years. Penicillin therapy of acute mastitis, the local application of penicillin ointment during lactation, some possible sources of the causative *Staphylococcus aureus,* and the resistance of some of the isolated bacteria to penicillin have been studied.

Penicillin Treatment of Acute Mastitis

Twenty-three consecutive patients with acute puerperal mastitis were treated only by the administration of penicillin. Of these patients, eleven were completely cured without any residual damage or lesions in the breast, six had residual or slowly subsiding induration, while the remaining six had localized abscesses, confirmed by incision and drainage. The dosage of penicillin was 20,000 units intramuscularly every three hours (8 times daily), except in three patients (Nos. 4, 5, and 9), who received 15,000 units every three hours. The total dosage of penicillin, number of days of treatment, duration of symptoms prior to therapy, the persistence of fever, and other facts relative to these patients are shown in Table I. On the average, the six patients who developed

TABLE I. RESPONSE OF MASTITIS TO PENICILLIN THERAPY

CASE	AGE	PARA	BREAST	DAY POST PARTUM	PENICILLIN*		SYMPTOMS (HOURS)	BECAME AFEBRILE (HOURS)	RESULTS
					TOTAL	DAYS			
1	20	i	Left	19	420,000	4	24	18	Good
2	20	i	Bilat.	12	800,000	5	48	48	Good
3	23	i	Right	9	435,000	4	24	36	Good
4	27	i	Right	8	340,000	5	48	24	Good
5	20	ii	Right	16	315,000	3½	12	12	Good
6	29	ii	Left	66	320,000	2	18	12	Good
7	30	ii	Right	8	700,000	5	12	6	Good
8	30	ii	Right	8	750,000	5	12	48	Good
9	33	ii	Left	12	240,000	3	24	24	Good
10	29	iv	Right	29	480,000	3	40	12	Good
11	29	iv	Left	71	750,000	5	24	6	Good
12	18	i	Right	26	960,000	6	9	48	Induration persisted
13	30	i	Right	150	210,000	4	72	24	Tenderness persisted
14	22	ii	Right	15	320,000	2	48	12	Induration persisted
15	23	ii	Right	28	780,000	6	12	12	Subsided slowly
16	32	ii	Left	45	850,000	6	96	36	Subsided slowly
17	24	iii	Right	29	960,000	6	36	48	Induration persisted
18	23	i	Left	14	800,000	5	36	24	Abscess—incised
19	24	i	Right	17	750,000	6	120	48	Abscess—incised
20	24	i	Right	10	230,000	2½	96	48	Abscess—incised
21	25	i	Left	42	530,000	5	144	36	Abscess—incised
22	29	ii	Left	12	640,000	4	24	24	Abscess—incised
23	20	iv	Right	16	640,000	4	96	24	Induration persisted
	Readmitted 2 weeks later				480,000	3			Abscess—incised

*20,000 units every three hours, 8 times daily, except cases Nos. 4, 5, and 9, dosage 15,000 units.

suppuration presented themselves late in the course of the disease, a fact which may explain in part the unfavorable results. In these six patients, symptoms had existed from 24 to 144 hours before the institution of penicillin therapy, whereas the longest period preceding treatment in the nonsuppurative cases was forty hours. The white blood cell count before therapy varied from normal to over 25,000 cells per cubic millimeter. All 23 patients became afebrile within forty-eight hours and two patients remained afebrile after six hours of treatment. The fact that patients became and remained afrebrile is not proof that the patient has been completely cured, as is shown by the development of abscess in six patients during treatment (Figs. 1 and 2). The white blood cell counts

became normal within a day or so in almost all instances. Although a local abscess remained, these patients felt greatly improved. As will be noted, Patient 23 was readmitted two weeks after the initial hospitalization and after discontinuance of penicillin therapy for drainage of the abscess. Another patient not included in the present group had a localized abscess for sixty days, during

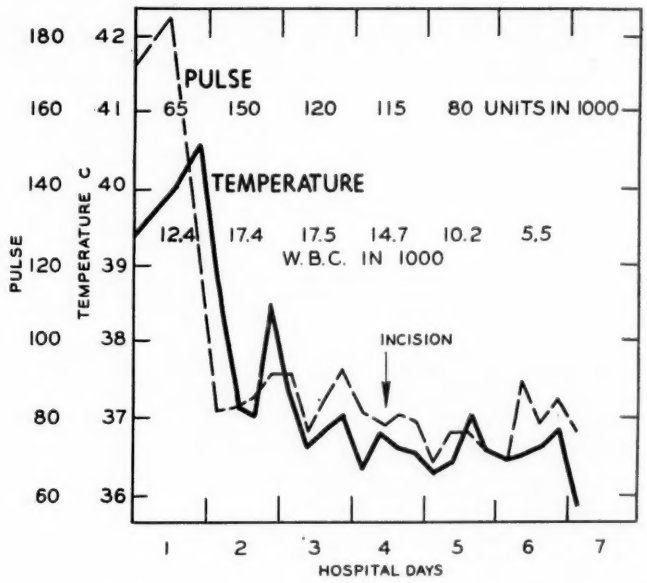

Fig. 1.—Penicillin in acute mastitis, six weeks post partum.

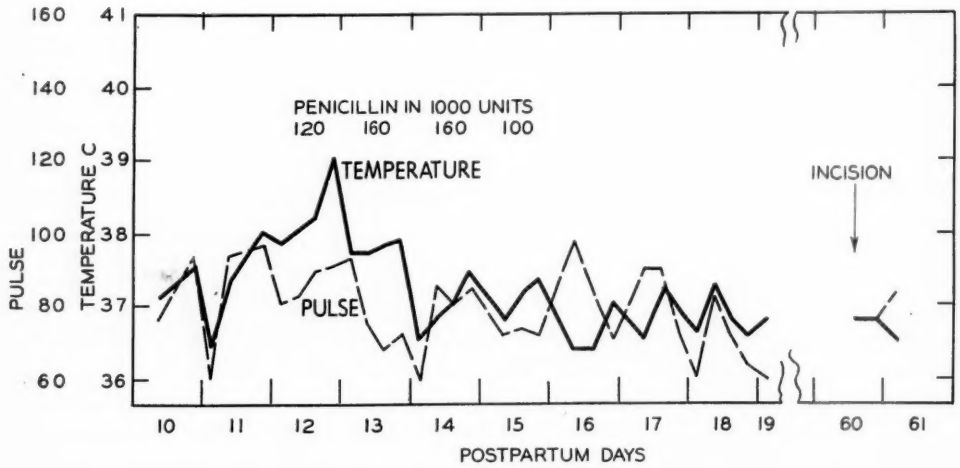

Fig. 2.—Penicillin in acute mastitis.

which time she was afebrile after the second day and maintained a normal white cell count. Cultures from five patients of the present series revealed staphylococci, four of which were hemolytic *Staph. aureus.* The fifth was identified as *Staph. albus.* The culture taken from the sixth patient (No. 19)

was unfortunately lost and a repeat culture was not obtained. It is thus apparent that with persistence of a gross lesion the patient must not be considered cured, and that in five of these six patients the staphylococci were able to survive in the local lesion during antibiotic therapy and to stimulate suppuration.

As will be remembered, it was necessary to use the sulfonamides within the first twelve to twenty-four hours in acute puerperal mastitis, if suppuration was to be avoided, and when it occurred during this therapy, suppuration was delayed for several days. Unlike the sulfonamides, penicillin did not increase the time required for abscess formation.

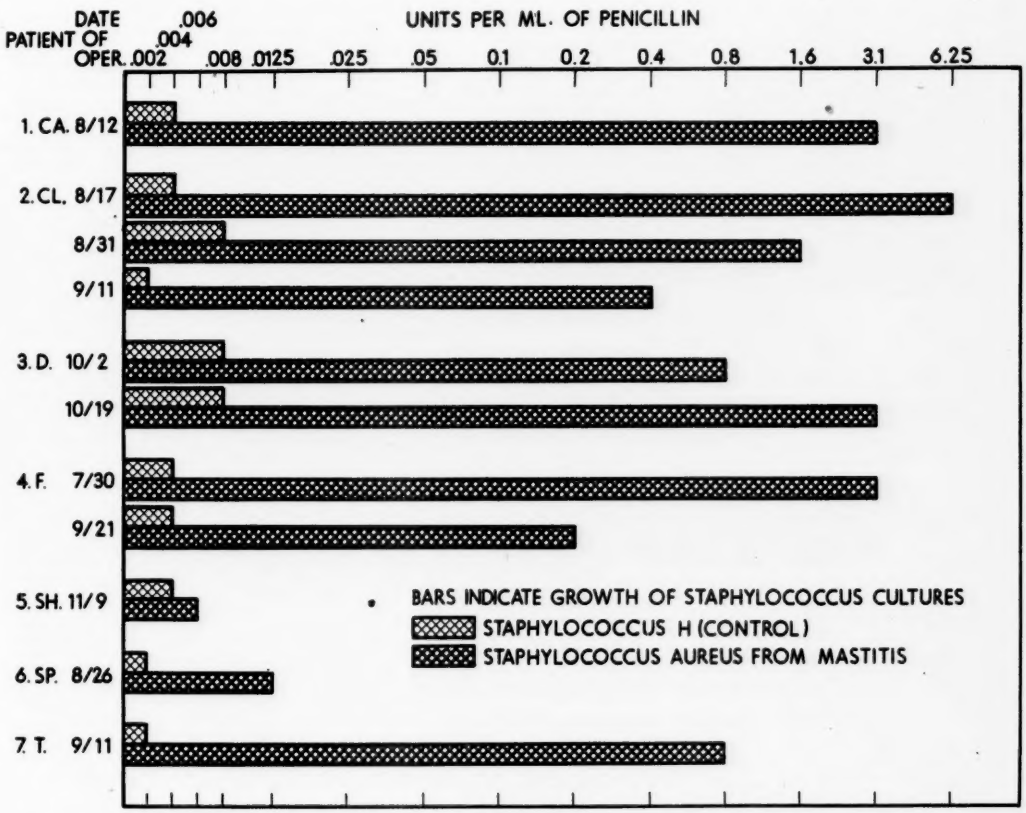

Fig. 3.—Resistance to penicillin of strains of *Staphylococcus aureus* from suppurative puerperal mastitis.

Penicillin Resistance of Staphylococcal Strains

The above observations suggested the desirability of studying the penicillin resistance of staphylococci isolated from breast abscesses. Consequently, staphylococci isolated from eleven abscesses occurring in seven patients were tested for penicillin resistance by the tube dilution method (Kolmer[3]) soon after their isolation. All of these cultures were hemolytic and coagulase-positive *Staph. aureus.* The results of these titrations are shown in Fig. 3. It will be observed that the resistance of these strains varied from 0.006 to 6.25 units per cubic centimeter of penicillin; seven cultures resisted a concentration of at least 0.8 units and four grew in 3.1 or more units of penicillin. The latter tolerances

exceed the anticipated levels of penicillin in the blood of patients treated by the usual dosages of antibiotic (Rammelkamp and Keefer[4]). In similar titrations the standard Oxford strain H of *Staph. aureus* resisted from 0.002 to 0.008 unit per cubic centimeter of penicillin. The observations do not indicate whether these staphylococcus strains were originally resistant to penicillin or whether resistance was acquired during antibiotic therapy. Furthermore, the barrier action of inflammatory tissue to passage of penicillin has not been investigated.

TABLE II. INCIDENCE OF WOMEN HAVING ONE OR MORE BREAST ABSCESSES IN COMPARISON TO THE NUMBER OF WOMEN DELIVERED ON A YEARLY BASIS AND THE AVERAGE FOR THE 13½ YEARS

YEAR	MOTHERS	ABSCESSES (TOTAL NO.)	PATIENTS HAVING ABSCESSES (NO.)	PATIENTS HAVING ABSCESSES (PER CENT)
1933-34	2,621	42	29	1.1
1934-35	2,909	29	24	0.82
1935-36	2,394	29	22	0.91
1936-37	2,341	10	7	0.29
1937-38	2,815	17	15	0.53
1938-39	2,718	31	18	0.66
1939-40	2,593	9	9	0.34
1940-41	2,827	11	10	0.35
1941-42	3,204	11	10	0.31
1942-43	3,766	17	13	0.34
1943-44	3,548	21	17	0.47
1944-45	3,431	16	13	0.37
1945-46	3,493	14	12	0.34
1946 (6 mo.)	1,969	15	11	0.55
Totals	40,629	272	210	0.51

TABLE III. NUMBER OF BREAST ABSCESSES BY MONTH FROM JULY, 1933, THROUGH JUNE, 1946, AND FROM JULY THROUGH DECEMBER, 1946, TO EVALUATE SPECIAL TREATMENT*

	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	JAN.	FEB.	MARCH	APRIL	MAY	JUNE	TOTAL
July, 1933, to June, 1946	26	16	15	10	16	24	21	13	18	12	16	12	
July-December, 1946	2	3	2	2	1	1							
13½ yr. quarterly totals		64			54			52†			40†		210
Average number per month		1.52			1.28			1.33			1.02		1.31

*Monthly averages are taken from quarterly totals.
†Only 39 months included in these entries.

The Prophylactic Use of Penicillin Ointment

A study has been made of the effect of the local application of penicillin ointment on the incidence of suppurative mastitis in nursing mothers. As a basis for comparison, a review has been made of suppurative mastitis in patients at the Chicago Lying-in Hospital from July 1, 1933, through Dec. 31, 1946 (Table II). The data include the number and percentage of patients developing abscess during each fiscal year. No account is made of the small, probably insignificant, percentage of patients who did not nurse their babies. It will be noted that the highest incidence of suppurative mastitis (1.0 per cent) occurred in 1933-1934, and that the lowest incidence (0.29 per cent) occurred in 1936-1937. During the entire 13½ year period, a total of 210 in 40,629 delivered

patients developed breast abscess, an incidence of 0.51 per cent. The total number of abscesses was 272. The incidence within the last six months (0.55 per cent) of the period under study was slightly higher than the average for the period (0.51 per cent) and higher than that encountered during the preceding two years (0.34 and 0.37 per cent yearly). In Table III the data are arranged by months. Of the 210 patients, 104 were seen between April and September and 106 between October and March. The lowest number per quarter-year occurred in April through June and the highest in July through September. The monthly incidence rates have not been calculated. The expected number of abscesses per month varied from about 1.0 to 1.5, the mean (arithmetic average) for the total period being 1.31 abscesses per month.

From July 1 through Dec. 31, 1946, the study of the prophylactic use of penicillin ointment was conducted. Only those patients who were lactating were included in the program. For this study the patients occupying rooms in the main building were divided into two groups (Table IV). Between July 1 and September 30, every nursing mother in both groups applied penicillin ointment to the nipples immediately after nursing. The ointment was a commercial preparation containing 1,000 units of the antibiotic per gram of oil base. The antibiotic potency was found to be maintained for at least ten days at room temperature during summer weather (August). The patients received approximately 2 Gm. of ointment (2,000 units of penicillin) at each treatment. Applications of ointment were started as soon as nursing was begun and were continued throughout the hospital stay and after the patient was discharged. The ointment was thus probably used for a total period of six to eight weeks, although application of ointment could be supervised only during the ten-day period of hospitalization. The rationale of the treatment was that local penicillin might prevent invasion and multiplication of staphylococci through the lacteal ducts. During the period, a total of 53 nonsuppurative and 18 suppurative cases of mastitis were observed in a total of 865 lactating mothers, an incidence of 6.1 and 2.0 per cent, respectively. The incidence rate of breast abscess was definitely higher than the average observed previously. It should be noted, however, that, in this study group, calculations of rates are based on the number of lactating mothers and not on total deliveries. From October through December, penicillin ointment was continued in Group I but was omitted in Group II, the only local care in the latter group being daily soap and water cleansing in the morning, and wiping with a clean dry cloth after nursing. The incidence of mastitis was essentially the same in the two groups. It is thus evident that the local use of penicillin ointment did not prevent the development of mastitis or of suppuration. The October-December study does not support the view that the use of ointment increased the incidence of mastitis.

TABLE IV. EFFECT OF PENICILLIN OINTMENT ON THE INCIDENCE OF NONSUPPURATIVE AND SUPPURATIVE MASTITIS IN LACTATING MOTHERS FROM JULY THROUGH DECEMBER, 1946

	LACTATING MOTHERS	NONSUPPURATIVE		SUPPURATIVE	
		NO.	PER CENT	NO.	PER CENT
Treated					
July-Sept. Groups I and II	865	53	6.1	18	2.0
Oct.-Dec. Group I	477	41	8.6	7	1.5
Untreated					
Oct.-Dec. Group II	388	27	6.9	5	1.3

During this period, patients who developed mastitis were immediately placed on parenteral penicillin therapy. Initially the dosage was 20,000 units every three hours, but after October 1 the dosage was increased to 40,000 units in an attempt to produce blood levels of 0.3 unit per cubic centimeter. The change was made because of the observed resistance to penicillin of a number of staphylococci isolated from breast abscesses.

Penicillin was not detected in the blood of 9 babies or 12 mothers as the result of use of penicillin-containing ointment on the breast following nursing.

TABLE V. FREQUENCY OF THE ISOLATION OF STAPHYLOCOCCUS AUREUS FROM THE NASOPHARYNX OF MOTHERS AND THEIR BABIES ON FIVE SAMPLINGS AFTER THE SECOND AND BEFORE THE TENTH POSTPARTUM DAY

CULTURE	MOTHERS																												
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
I												+				+			+	+					+	+			N	
II															+			+	+	+				+		+			N	
III			+					+				+	+			N		N								+			N	+
IV	+												+	+	+								+	+		+			N	
V					+			+				+		+		+	+	+	+	+		+				+			N	

	NEWBORN OF CORRESPONDING MOTHERS																													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
I		+											+					+												+
II		+			+	+		+		+					+		+	+	+											+
III		+			+	+		+		+	+		+		+			+	+			+					+			+
IV		+	+	+	+	+	+	+		+	+		+		+			+	+			+					+			+
V		+	+	+	+	+		+		+	+	+	+	+	+			+	+	+	+	+					+			+

+ = *Staphylococcus aureus* isolated which is coagulase positive and hemolytic.
N = *Staphylococcus aureus* isolated which is coagulase positive but nonhemolytic.

Resistance to Penicillin of Nasopharyngeal Staphylococci From Mothers and Infants

Inasmuch as it is known that the nasopharyngeal cavity is a common source of *Staph. aureus,* a cultural study of the nasopharynx for this organism was undertaken. Also, it is known that newborn infants usually acquire a bacterial flora in the upper respiratory tract within the first forty-eight hours of life. According to the work of Torrey and Reese,[8] this flora results from association with the mother and attendants. These workers noted that 50 per cent of the newborn infants had *Staph. aureus* after the second day of life. The frequency of isolation of *Staph. aureus* in the present series is shown in Table V. Five different cultures were taken from each mother and each baby between the second and tenth postpartum days. In the table, the Roman numerals represent the order of the five successive cultures, and the Arabic numbers indicate the corresponding pairs of mothers and babies. The positive sign indicates isolation of a coagulase-positive and hemolytic strain, and the N means that the isolated staphylococcus was coagulase-positive but nonhemolytic on blood agar plates. The ability of staphylococcus cultures to coagulate blood plasma and to hemolyze red blood cells correlates closely with toxin production and pathogenicity. Material for culture was obtained by means of sterile, small applicators, which were passed through the nares of the infants and mothers. Colonies isolated on plate cultures were studied for the development of pigment, the hemolysis of erythrocytes, and the coagulation of human blood plasma by the usual methods. Twenty-one of 30 babies were found to harbor *Staph. aureus* in the nasopharyngeal passage on at least one occasion. In other words, over two-thirds of the babies were found to have potentially pathogenic

staphylococci in the nasopharynx within the first ten days of life. It is interesting that staphylococci were found in 20 of the 30 mothers, but less frequently in the series of cultures. By inference it seems likely that the nursing baby is a source of infection in puerperal mastitis. Final proof of this hypothesis is hindered by the difficulty of identification of staphylococcus strains. Other possible sources of infection include the skin and the lower genital and intestinal tracts of the patients or contacts.

The penicillin resistance of 60 nasopharyngeal strains of staphylococci was determined (Fig. 4). These cultures were from 29 mothers and 31 babies. It is evident that 7 of the 31 strains from babies were resistant to 0.5 or more units per cubic centimeter of penicillin, as were 3 of the 29 strains from the mothers.

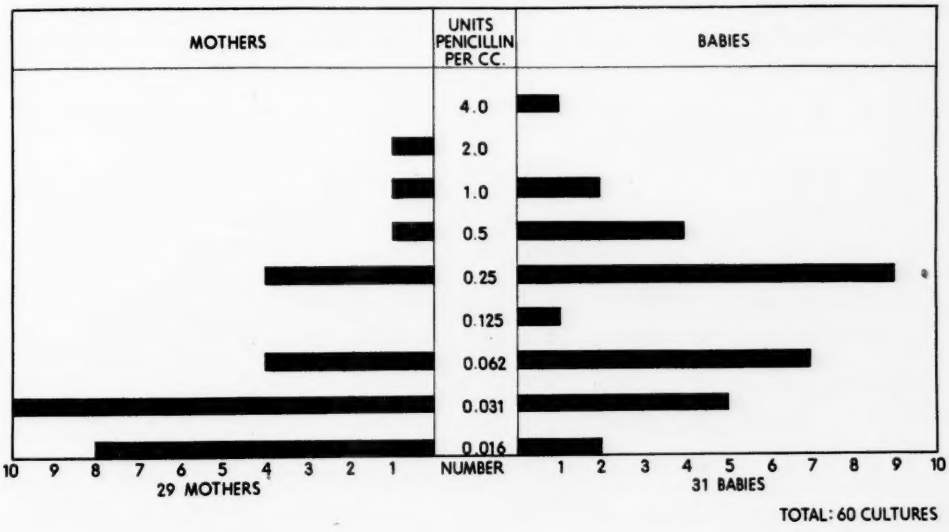

Fig. 4.—The degree of resistance to penicillin by the *Staphylococcus aureus* isolated from the nasopharynx of mothers and their babies after the second and before the tenth postpartum day.

Discussion

The present work indicates that infection of the breast may occur in lactating mothers from the patient herself or from the nursing infant. Contributing factors, such as trauma to the nipple or breast tissue, which we believe to favor the development of mastitis, have not been evaluated in the present study. Although our results suggest the importance of the nasopharynx, other possible sources of infection must, of course, be recognized, and these have not been eliminated in the present series of patients.

The staphylococcus cultures isolated from breast abscesses and from nasopharyngeal cultures of mothers and infants varied considerably in susceptibility to penicillin, but some strains from all sources had a significantly high resistance to the antibiotic. This resistance would appear to be a factor in the development of suppuration during penicillin treatment of some patients having mastitis, and should be considered in the determination of "adequate" penicillin therapy.

Thus, Rammelkamp and Kirby[5] found that 25,000 units of penicillin given intramuscularly every two hours would produce optimum continuous levels in the blood for staphylococcus infection. They further state that the continuous intravenous infusion method, using 100,000 units per twenty-four hours should produce a level of 0.1 units per cubic centimeter, and 400,000 units would yield an average level of about 0.4 units per cubic centimeter, whereas subcutaneous administration resulted in only one-half as great a level. The observations by Goerner, Geiger, and Blake[6] compare reasonably well. By contrast, Gerber, Shwartzman, and Baehr[7] found a peak of 6 units per cubic centimeter following 100,000 units given intramuscularly. Accordingly, a peak blood concentration of 2 units would require not less than 33,000 units and probably more than 50,000 units every three hours. From their data, it would appear that sustained blood levels of 2 units per cubic centimeter would not be obtained by the customary dosages, and that the usual penicillin blood levels would be sufficient only if the causative microorganism is particularly susceptible.

Progression of the disease process to suppuration and the necessity for incision and drainage in a number of patients in our series indicate the inability of penicillin treatment to arrest the infection in some instances. Late treatment, the resistance of some staphylococcal strains to penicillin, and the localizing effect of the inflammatory tissue would seem to contribute to this reaction. Increased dosage of penicillin seems desirable for infections with organisms of higher than usual resistance to the antibiotic. The use of penicillin ointment locally on the nipple after nursing was in this study an unsatisfactory prophylactic measure against puerperal mastitis.

It should perhaps be emphasized that puerperal mastitis is a serious medical complication of the puerperium. It is also psychologically disturbing to the patient and may create a complex problem when these mothers must be readmitted to the hospital for treatment.

Conclusions

A report is made of observations of a total of 210 patients having suppurative puerperal mastitis. Suppuration was observed in 6 of 23 consecutive mastitis patients receiving penicillin therapy.

Eleven strains of staphylococci isolated from suppurative mastitis grew in the presence of from 0.006 to 6.25 units per cubic centimeter of penicillin. A significant proportion of these strains were resistant to the antibiotic, since four grew in at least 3.1 units per cubic centimeter.

The local use of ointment containing penicillin after nursing failed to affect the incidence of mastitis in postpartum patients. The incidence of mastitis in lactating patients receiving local treatment with penicillin is compared with that in a control group over a three-month period and with an uncorrected incidence of suppurative mastitis in the Chicago Lying-in Hospital during the past thirteen years.

Nasopharyngeal cultures from mothers and babies were examined for *Staphylococcus aureus*. Twenty-one of 30 babies were found to harbor *Staph.*

aureus during the first ten days of life, as were 20 of the 30 mothers. Ten of these staphylococcal strains were resistant to 0.5 or more units per cubic centimeter of penicillin in vitro. The significance of these findings to the source of infection in puerperal mastitis is discussed.

We thank Schenley Laboratories, Inc., for generously supplying all of the penicillin ointment for that part of the study.

References

1. Hodgkinson, C. P., and Nelson, R. E.: J. A. M. A. **129**: 269, 1945.
2. Power, H. A., and Cravotta, C. A.: Am. J. Obst. & Gynec. **51**: 230, 1946.
3. Kolmer, J. A.: Penicillin Therapy, New York, 1945, D. Appleton-Century Co., Inc.
4. Rammelkamp, C. H., and Keefer, C. S.: J. Clin. Invest. **12**: 425, 1943.
5. Rammelkamp, C. H., and Kirby, W. M. M.: Bull. N. Y. Acad. Med. **21**: 656, 1945.
6. Goerner, J. R., Geiger, A. J., and Blake, F. G.: Ann. Int. Med. **23**: 491, 1945.
7. Gerber, I. E., Schwartzman, G., and Baehr, G.: J. A. M. A. **130**: 761, 1946.
8. Torrey, J. C., and Reese, Martha K.: Am. J. Dis. Child. **68**: 208, 1945.

Discussion

DR. FREDERICK H. FALLS.—It becomes necessary to evaluate the use of penicillin in the various infections that arise in pregnant women. It is important that Dr. Hesseltine has made a careful study of penicillin as far as puerperal mastitis is concerned. I agree with him as far as our experience has gone, but we have not made as perfect a study as he has. We have used penicillin in a considerable number of cases of puerperal mastitis.

It would seem from the study that 0.51 per cent is a rather high incidence of mastitis. In our clinic, though I have not the figures, I am sure it is not quite that high. I think the more breasts are left alone the less mastitis will occur. Formerly, at the Lying-in Hospital, as soon as a patient was delivered, the breasts were scrubbed, alcohol and bichloride of mercury were applied, and they were kept absolutely clean by sterile dressings, and I have never before or since seen so many breast abscesses. The lesson to be learned is to leave the breasts alone. Do not irritate them and thus produce cracks that will permit staphylococci to enter. As Dr. Hesseltine pointed out, that is the organism you expect to find, but in some abscesses, on culture, streptococci were noted.

It is important to stress the alterations in the clinical picture of this disease as well as other diseases of the puerperal woman which accompany the use of penicillin; in fact, we must learn the history of acute puerperal mastitis all over again. These drugs alter the clinical course, as Dr. Hesseltine pointed out, and we can have pus in the breast and still have a normal temperature and normal leucocyte count. That was not the case some time ago, but it is now, and we have to take those things into consideration. Two-thirds of these mothers were found to have staphylococci in nose and throat. That is a powerful argument against a good deal of thinking of how clean are the nurseries and how clean are the places where these patients are delivered, and how important it is to segregate these patients. If these patients have virulent staphylococci in the nose and throat, we bring those noses and throats into the delivery room and spread the staphylococci.

It is important also to realize that breast abscess may have a serious general effect on the patient. When I was a resident at the Lying-in Hospital, we had one patient who was admitted with a breast abscess at 7 o'clock at night, the abscess was opened at 7:30 P.M., and she was dead the next morning. We had another patient in whom a breast abscess was opened in May, and the following July she died of general peritonitis following a perforation of an ulcer of the colon. So breast abscesses are not only local infections, but they have general implications.

Also important is the fact that the more attention paid to the general well-being of the patient, the less chance there is of having any type of infection. Careful prenatal care and improvement of the general health will reduce the susceptibility to these organisms. I do not think the organisms all come entirely from the nose and throat of the mother or of the baby.

It is just as important to look in the ward for the patient who has acne or some other type of staphylococcic skin lesions, or the nurse with the paronychia, or the intern with a boil on the neck.

I should like to have heard a little more about the care of breast abscess and about the surgical opening of breast abscess. This disease is different from any other because the pus is located in the septa of the breast. That is why you have to wait until these abscesses form. If you open them early, there is poor drainage. An abscess around the areola is easier to open than one that is away from it; the latter is very difficult.

DR. JAMES E. FITZERALD.—Mastitis is not necessarily limited to the puerperium, as one death occurred in Chicago in a woman seven months pregnant. This patient had a bilateral suppurative mastitis which terminated fatally in spite of drainage.

I am rather intrigued by Dr. Hesseltine's results in the prophylactic use of penicillin ointment which increased the incidence of suppurative mastitis by 400 per cent. I am impressed by the low incidence of suppurative mastitis in 1927-1937 which was before penicillin and before there was much refinement of the sulfonamides. It is not reasonable to suppose that our technique in the care of lactating breasts was superior at that time.

There seems to be a marked decrease in the incidence of breast infections over a period of years, and the explanation is not forthcoming. Twenty years ago infected breasts that required surgical drainage were so common that Hillis rigged up an enormous bell jar to fit over the breast so that he could use a partial vacuum for continuous drainage. Yet in the past three years only 60 breasts have required drainage. During that time we have delivered approximately 20,000 patients. This makes an incidence of about one-third of one per cent and a considerable number of patients were delivered elsewhere, which would decrease the incidence considerably. The low incidence is not due to better technique, because nursing shortage has made this impossible. It must be remembered that practically all of these patients breast feed their babies. It is also noteworthy that these patients have been sent home very early because of bed shortage.

This makes a very confused picture and I do not believe that our good results in the past few years are due to the fact that every suspicious breast infection is treated immediately with both penicillin and sulfonamides.

I have learned from Dr. Hesseltine's paper that lactating mothers may develop mastitis, that such breasts may suppurate, and that when they do suppurate, bacteria may be cultured from the pus. I would be more impressed if I could learn how to prevent the complication.

DR. HESSELTINE (Closing).—In answer to Dr. Fitzgerald, the average for the entire period of the study, thirteen and one-half years, was 0.51 per cent. The figure for the last six months of the period was 0.55 per cent; during that time we checked every patient and deleted every patient who did not nurse or lactate during that time.

OVARIAN DYSFUNCTION IN YOUNG WOMEN TREATED WITH LOW-DOSAGE IRRADIATION

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BEFORE 1927 at the Mayo Clinic, when a young woman confronted us with the problem of functional menstrual irregularity, we could only advise that she maintain her weight at what was normal for her on a well-balanced diet, get plenty of out-of-door exercise, and avoid nervous tension. In addition to such general measures, if we found the basal metabolic rate to be lower than normal, we would suggest raising the rate to around –3 per cent by administration of thyroid extract and maintaining it at this level for several months, hoping to correct the menstrual disturbance. Sometimes ovarian extracts were prescribed with little hope of success.

About 1925 there began appearing in the German literature reports of the use of roentgen rays over the ovaries in the treatment of the functional menstrual disturbances with benefit. In cases of amenorrhea, the menses had been re-established. Rubin[1] in New York soon reported similar results. It was decided to try this treatment at the Clinic. We used extreme caution at first, irradiating only one ovary according to the technique of Rubin.

On Jan. 1, 1927, a woman from Canada registered at the Clinic. She was 32 years of age, was 5 feet 1½ inches (about 156 cm.) in height and weighed 213 pounds (about 97 kilograms). She had been married for seventeen years and had never been pregnant. She said her menses began when she was 11 years of age, were fairly regular for eleven years, lasting three days with an amount of flow necessitating use of three napkins a day. She had had much pain with the menses from the onset. The pain was present for several days before and all during the period. From the time she was 22 years old till the time of her examination her periods had been irregular, occurring from one to eight or nine months apart, and she had not menstruated for two years when she presented herself. She complained of hot flushes.

Aside from obesity, the general physical examination revealed no abnormalities. Pelvic examination gave negative results. Her basal metabolic rate was +15 per cent and the roentgenogram of the sella turcica showed no abnormality. She was given low-dosage roentgen therapy over one ovary and was told to take 10 grains (0.65 Gm.) of ovarian extract three times a day for the same two weeks each month. Her periods began the fifth day after the roentgen treatment and occurred regularly until August, when she became pregnant. After a full-term pregnancy she was delivered of a baby who was reported by the doctor to be normal in every way, but the child died shortly after birth, of respiratory failure.

The patient's periods continued to occur regularly and, the next year, another full-term pregnancy resulted in the birth of another normal infant in August, 1929. In 1933, when we last heard from her, she said that this child was alive and well. The patient's menstrual periods had been regular for a year after the second childbirth, when they ceased again in 1930.

Our good fortune in establishing regular menses in this case encouraged us to continue to use low-dosage irradiation. It has proved the most dependable means at hand of re-establishing the menses after a period of amenorrhea and of continuing the menses regularly for a few months, a sufficient time to allow the patient to become pregnant.

Irradiation in the Treatment of Ovarian Dysfunction

Before the availability of the more potent ovarian hormones, we used thyroid extract and low-dosage irradiation for several years in treatment of the functional menstrual irregularities. In the menometrorrhagic type, administration of thyroid was helpful when it could be used, but we soon found that low-dosage treatment with roentgen rays was only a temporary help (Table I) and sometimes increased the bleeding, so we had to turn to other measures such as curettage and intrauterine administration of small doses of radium. Radium probably acted on the endometrium as well as on the ovaries, for we noted that usually the periods would cease altogether for two to six months, depending on the dosage used, and then return and be rather regular for a time. Low-dosage roentgen irradiation then came to be used almost exclusively for the amenorrheic type of ovarian dysfunction. By "amenorrheic type," we mean dysfunction in which there is a tendency to longer than normal intervals between the menstrual periods and a decrease in the flow or complete absence of menstruation.

For treatment of this type of ovarian dysfunction, we at the Clinic continue to radiate one field over each temporal region, centering over the pituitary, and two fields over the front of the abdomen, centering over each ovary. The following technique is used: 200 kilovolts, 20 milliamperes, 0.75 mm. copper and 1 mm. aluminum filters, 50 cm. distance, for five minutes. This represents approximately one-sixth of a skin erythema dose. In some cases to be described later the treatment is not given over the pituitary.

TABLE I. DATA CONCERNING PATIENTS TREATED FOR MENOMETRORRHAGIA BY IRRADIATION, 1927 TO 1940, INCLUSIVE

	MARRIED PATIENTS	UNMARRIED PATIENTS	TOTAL
Treatment:			
Irradiation only	5	5	10
Irradiation and estrogen	8		8
Irradiation and hormones		5	5
Irradiation and snake venom		1	1
Irradiation, snake venom and Proluton*	1		1
Irradiation, antuitrin S and thyroid extract	1		1
Total	15	11	26
Results:†			
Improved temporarily	12	7	19
Not improved	3	4	7
Periods regular	6	4	10
Periods irregular	9	7	16
Menorrhagia	6	5	11
Pregnancies (full term)	3		3
Miscarriages	1		1
Pregnancies directly after treatment	1		1

*Progesterone.
†Two years after treatment.

Clinical Observations

Among cases in which patients complained of a tendency to amenorrhea and in which they had already ceased to menstruate, we early distinguished clinically two groups—one group of patients who had no complaints aside from the menstrual irregularity and perhaps a tendency to gain weight during the periods of amenorrhea and the other group who had many complaints associated both with their periods when they had them and with the periods of amenorrhea. The symptoms of which they complained were similar to those which women experience with the physiologic ovarian failure of the early climacterium. Those cases in the first group in which symptoms were not associated with amenorrhea we thought were cases of pituitary failure, and the cases in the second group in which young women had symptoms similar to those of the climacterium we classified as cases of primary ovarian failure. Later on, in the laboratory, we had the satisfaction of substantiating our clinical impressions with determinations of the amount of gonadotropin from the anterior lobe of the pituitary and estrogenic substances in the urine.

In cases of pituitary failure, the gonadotropic hormone, as a rule, is not found in the urine and if the failure is complete, at least temporarily, no estrogens can be demonstrated. When the failure is not complete small amounts of estrogen are frequently present. In cases of ovarian failure, gonadotropic hormone is found in greater than normal amounts and estrogen may or may not be found according to the degree of failure.

Clinically, cases of ovarian dysfunction due to pituitary failure outnumber those due to failure primary in the ovaries, for pituitary function is easily disturbed by general systemic conditions, including changes in dietary habits as well as disease states, and most frequently by emotional upsets. These general systemic or psychic disturbances can effect a change in pituitary function and secondarily induce menstrual irregularities at any time during the woman's menstrual life, but the young women are more prone to such disturbances, as their nervous systems are more unstable and their food habits more irregular. Pituitary dysfunction, secondary to some general disturbance, is easily remedied if the consequent amenorrhea has not lasted long enough to bring about much atrophy of the uterus. The uterus atrophies rapidly with pituitary failure if it is complete enough to induce complete cessation of ovarian function.

In addition to this group of women who have pituitary failure secondary to some general systemic disturbance, there is a group who apparently have an endogenous pituitary dysfunction due to lack of functional development of the gland or to some disturbance of undeterminable etiology. In this type of case the history of the menstrual irregularity frequently dates back to the onset of the menses or follows parturition. It is more difficult to effect an improvement with treatment in these cases.

In cases of primary pituitary dysfunction, the basal metabolic rate is usually lower than normal and the patient tends to put on weight during the periods of amenorrhea. In pituitary failure it is considered that the ovaries are adequate but dormant and, as one would expect, when these girls have a period it is likely to be quite normal and without molimina.

Ovarian dysfunction due to a failure which is primary in the ovaries is the result of poorly developed ovaries or retained follicle or corpus luteum cysts. Here again the menstrual irregularity may date back to the onset of menstruation or follow parturition. The regularity of the cycle seems most disturbed in the pituitary type of failure.

When pituitary function is good and ovarian function is poor, the periods tend to be more regular and, though periods may be missed entirely, molimina are often present at the regular menstrual time. Likewise some estrogen is usu-

ally present in the blood and urine. Contrary to the general impression, the content of estrogen in the urine may be higher than normal when the pituitary is hyperfunctioning and cystic follicles are present. In these cases, endometrial biopsy reveals a persistent proliferative type of endometrium and no pregnanediol is found in the urine. There is less tendency to uterine atrophy in cases of ovarian failure, unless the failure is complete and the amenorrhea has been present for a long time.

The reason for believing that many of the menstrual irregularities complained of by the younger women have a developmental basis is that they date back to the onset of menstruation and often right themselves if the young woman can be carried along to the age of approximately 23 or 24 years, when glandular development is complete.

Study of 331 Cases

We have reviewed the histories of 430 cases of typical functional menstrual irregularities treated here at the Clinic during the years 1927 to 1941. Ninety-nine cases are not included in this study. A small group was omitted because the patients had some systemic disease (diabetes, rheumatoid arthritis, or tuberculosis) which, though it seemed well controlled at the time of the treatment, had no doubt been a factor in the initiation of the amenorrhea. The others were left out because the follow-up information was either not obtainable or was unsatisfactory, or because they were more than 32 years of age. I wished in this study to include only the younger women. This left 331 cases which have been grouped as the tables indicate.

It seemed advisable to separate the patients treated primarily for amenorrhea into two groups, those single and those married at the time of treatment. Among the married women, we were interested especially in the direct effect of irradiation on the sterility associated with ovarian dysfunction. As is well known, a high percentage of these women are sterile. We wished to determine whether treatment was worth while when the amenorrhea had been present for more than one year, so the cases of amenorrhea were subdivided again into those in which the period of amenorrhea was less than a year and those in which the period of amenorrhea was more than a year.

In the whole group of single women treated with irradiation from 1927 to 1941, inclusive, for an ovarian dysfunction of the amenorrheic type, there were 136 in all. In 63 of these, the dysfunction was considered to be primary in the pituitary and in 73 primary in the ovaries.

In 46 (73 per cent) of the group of 63 cases of pituitary failure, regular menses were re-established directly after treatment. Two patients had only temporary improvement. In the other cases the improvement continued for more than one year. The dysfunction of 9 young women, as will be noted in Table II, did not improve after the irradiation therapy, but later on the menses returned spontaneously.

In 48, or 66 per cent, of the group of 73 cases in which the menstrual irregularity was considered to be due to primary ovarian failure, regular menses were re-established. In seven, only temporary improvement was achieved. In the others, menstruation continued to be regular for one year at least. Fourteen young women who received no benefit from irradiation began to menstruate later, spontaneously.

When the period of amenorrhea was more than one year, in only about 44 per cent of the cases of primary ovarian failure was improvement noted and this lasted only three months in four cases in which irradiation only was used. In the cases of amenorrhea due to pituitary failure that had been present for more than one year, improvement was noted in about 62 per cent and temporary

TABLE II. RESULTS OF TREATMENT OF 136 YOUNG UNMARRIED WOMEN* FOR MENSTRUAL IRREGULARITY, 1927-1940, INCLUSIVE

	PITUITARY FAILURE			OVARIAN FAILURE		
	DURATION OF AMENORRHEA			DURATION OF AMENORRHEA		
	LESS THAN 1 YR.	1 TO 4½ YR.	TOTAL	LESS THAN 1 YR.	1 TO 10 YR.	TOTAL
Irradiation only:	19	12	31	38	23	61
Improved only 3 mo.	2		2	3	4	7
Improved for 1 yr. at least	17	7	24	24	5	29
Irradiation, thyroid extract, and estrogens:	20	12	32	10	2	12
Improved for 1 yr. at least	14	6	20	10	2	12
Total not improved immediately after treatment	8	9	17	11	14	25
Menses returned later, spontaneously	4	5	9	7	7	14
Total patients treated	39	24	63	48	25	73
Total improved	31	15	46	37	11	48

*Patients less than 32 years old. Average age: 22.5 years.

improvement occurred in fewer cases. This makes it evident that the sooner young women who have amenorrhea are treated, the better the chance of re-establishing and continuing the menses.

To a group of the young women treated for menstrual irregularity while single from 1930 to 1941, questionnaires were sent out in 1945. We asked them simple questions relative to their general health, the regularity of their menses, whether they had married, if they had been pregnant and, if so, how many children they had had. Fifty-five answered the questions intelligently and the results are given in Table III. Twenty-one women were still single. Twelve of

TABLE III. FOLLOW-UP STUDY OF FIFTY-FIVE PATIENTS* WHO WERE UNMARRIED WHEN TREATED FOR AMENORRHEA IN THE YEARS FROM 1930 TO 1940, INCLUSIVE; INFORMATION OBTAINED BY QUESTIONNAIRE IN 1945

	PATIENTS UNMARRIED IN 1945					PATIENTS MARRIED IN 1945				
	PITUITARY FAILURE		OVARIAN FAILURE			PITUITARY FAILURE		OVARIAN FAILURE		
	DURATION OF AMENORRHEA†					DURATION OF AMENORRHEA†				
	LESS THAN 1 YR.	1 TO 10 YR.	LESS THAN 1 YR.	1 TO 10 YR.	TOTAL	LESS THAN 1 YR.	1 TO 7 YR.	LESS THAN 1 YR.	1 TO 7 YR.	TOTAL
Irradiation only	2	5	3	2	12	8	2	14	4	28
Irradiation, thyroid extract and estrogens	3	2	3	1	9	2	1	2	1	6
Total treated	5	7	6	3	21	10	3	16	5	34
Improved	2	2	6	2	12	9	1	13	1	24
Not improved	3	5	0	1	9	1	2	3	4	10
Periods regular	3	5	5	1	14	7	1	16	2	26
Periods irregular	2‡	2‡	1	2‡	7	3	2‡	0	3	8
Patients pregnant						8		15	2	25
Full-term pregnancies						12§		23	3	38
Miscarriages						1		0	1	2
Patients married and pregnant within 1 yr. after treatment								4		4

*Average age of patients at time of treatment: 23.4 years.
†Before treatment.
‡One patient was having no menstrual periods.
§One patient gave birth to a monster.

these women stated that menstruation had become more regular after treatment; 14 stated their periods were regular. Seven related that their periods were still irregular, and 3 of these who were amenorrheic when treated had not had any period since treatment. Thirty-four women had married. Twenty-four of these stated their menses had become more regular after treatment; 26 reported that they were having regular periods in 1945; 25 women had been pregnant and had had 40 pregnancies. Two of these had ended in miscarriages. One patient gave birth to a monster. This long-range study of low-dosage irradiation in young women makes us feel that there is no late harmful effect on the ovaries.

As I have stated, the goal to be approached in treatment of young married women complaining of menstrual irregularity and sterility is the establishment of regular periods until pregnancy can take place. It was assumed by all these women that they were responsible for the sterility. In most of the cases the husband was not with the patient when she was at the Clinic and we have no way of knowing which was sterile. This study would be more valuable if this were known. Any young married woman who has abnormal menses and is childless feels sure she is to blame for the sterility and usually will go to any length to correct it. In the results of this study, pregnancy has been considered to have been made possible by treatment if the patient became pregnant within three months after regular menses were established. Subsequent pregnancies have not been counted.

Of one group of 62 women who were married when treated, we have sufficient clinical records (over several years in the majority of cases) so that a questionnaire in 1945 was not deemed necessary. Data concerning these patients are given in Table IV. Forty-two of the women were improved with treatment and 36 continued to have regular periods; 19 became pregnant directly after treatment, and 3 of these pregnancies were terminated early in abortion. One woman in this group had 3 roentgen-ray treatments over a period of years and pregnancy directly followed each treatment.

TABLE IV. FOLLOW-UP STUDY OF CLINICAL RECORDS OF SIXTY-TWO PATIENTS WHO WERE MARRIED WHEN TREATED FOR AMENORRHEA, 1927-1940 INCLUSIVE

	PITUITARY FAILURE			OVARIAN FAILURE*		
	DURATION OF AMENORRHEA			DURATION OF AMENORRHEA		
	LESS THAN 1 YR.	1 TO 6 YR.	TOTAL	LESS THAN 1 YR.	1 TO 6 YR.	TOTAL
Irradiation only	13	3	16	20	3	23
Irradiation, thyroid extract and estrogens	7	3	10	7	6†	13
Total treated	20	6	26	27	9	36
Improved	15	2	17	21	4	25
Not improved	5	4	9	6	5	11
DATA OBTAINED 1 TO 9 YEARS AFTER TREATMENT						
Periods regular	14	2	16	16	4	20
Periods irregular	6	4	10	11	5	16
No periods	5	3	8	9	4	13
Patients pregnant after treatment	7	2	9	8	2	10
Full-term pregnancies	6	2	8	8	5	13
Miscarriages	3‡		3	2	1	3
Patients pregnant directly after treatment	5	2	7	8	4	12

*Average age of patients: 27.3 years. Average period of sterility prior to treatment: 5.7 years.

†One patient had three treatments and pregnancy followed each.

‡Pregnancy followed treatment.

A second group of 61 women who were married when treated from 1927 to 1940, inclusive, were sent questionnaires in 1945 and reported as follows: Forty stated their menstrual periods had become more regular after treatment; 39 said their periods were regular in 1945; 26 had been pregnant; 15 became pregnant directly after the treatment; two pregnancies had terminated in abortion and one woman had had a tubal pregnancy. To 1945 the 26 women who became pregnant had had 46 full-term pregnancies, 5 miscarriages, and 2 tubal pregnancies. Additional information is given in Table V.

TABLE V. FOLLOW-UP STUDY OF SIXTY-ONE PATIENTS* WHO WERE MARRIED WHEN TREATED FOR AMENORRHEA IN THE YEARS FROM 1927 TO 1940, INCLUSIVE; DATA OBTAINED BY QUESTIONNAIRE IN 1945

	PITUITARY FAILURE			OVARIAN FAILURE		
	DURATION OF AMENORRHEA			DURATION OF AMENORRHEA		
	LESS THAN 1 YR.	1 TO 7 YR.	TOTAL	LESS THAN 1 YR.	1 TO 7 YR	TOTAL
Irradiation only	10	8	18	14	6	20
Irradiation, thyroid extract and estrogens	6	5	11	11	1	12
Total treated	16	13	29	25	7	32
Improved	12	4	16	21	3	24
Not improved	4	9	13	4	4	8
DATA OBTAINED IN 1945						
Periods regular	14	4	18	18	3	21
Periods irregular	2	9	11	7	4	11
No periods	1	6	7	4	4	8
Patients pregnant after treatment	8	3	11	12	3	15
Full-term pregnancies	16	4	20	22	4	26
Miscarriages and ectopic pregnancies	3†‡	2†	5	1‡		1
Pregnancies directly after treatment	5	2	7	6	2	8

*Average age: 28.2 years. Average period of sterility prior to treatment: 4.9 years.
†Two patients became pregnant shortly after treatment.
‡One ectopic pregnancy.

In summary, of 123 young married women treated with low-dosage irradiation, 34 (27.6 per cent) had become pregnant directly after treatment. Eighty-two women stated their menstrual periods were definitely more regular after treatment and, of these, 45 had been pregnant and had had 67 full-term pregnancies, 10 abortions, and 2 ectopic pregnancies; one patient gave birth to a monster after a full-term pregnancy.

Low-dosage irradiation for dysmenorrhea with regular, normal menses was given to 24 women (Table VI); 18 were improved for six months, and 8 for at least two years. One young woman became pregnant directly after the treatment. None of these young women complained of any menstrual irregularity after treatment. Several requested repetition of the treatment which had given relief several times. The effect would usually last about six months and then treatment would have to be repeated. Fearing this repetition of treatments, we stopped advising it.

Twenty-two women who had regular, normal menses and were sterile and whose husbands' fertility had been checked and found within normal limits by the criteria used previous to the last five years (no morphologic study) were given low-dosage irradiation over the pituitary and ovaries (Table VI). Eleven received pregnancy serum in addition to irradiation and 5 others were given estrogen and progesterone in addition. Three became pregnant but only 2 preg-

nancies occurred directly after treatment. Six women complained of irregularity of periods after treatment. These were the only patients of the whole group treated with irradiation who made complaints about the treatment.

It does not seem wise to treat women for sterility alone with low-dosage irradiation. The sterility in these cases apparently is not dependent on ovarian dysfunction.

TABLE VI. DATA CONCERNING FORTY-SIX PATIENTS WHO HAD NORMAL MENSTRUAL PERIODS AND WERE GIVEN IRRADIATION FOR ANOTHER CONDITION IN THE YEARS 1927 TO 1940, INCLUSIVE

	DYSMENORRHEA	STERILITY
Patients	24	22
Average age, years	25.7	28.4
Average period of sterility, years		5.1
Irradiation only	19*	6†
Irradiation and hormones	5	16‡
Improved for 6 months	18	
Improved for at least 2 years	8	
Pregnancies		3
Patients pregnant directly after treatment	1	2

*Seven of these nineteen women had two treatments. Two women had ten treatments each.

†Three of these women had two treatments.

‡Eleven women received pregnancy serum in addition to irradiation and hormones (estrogen and progesterone).

Comment

In treatment of functional menstrual irregularities, the object is to try to establish more regular normal menses and continue these until pregnancy can take place. Pregnancy is often a stimulus to the endocrine glands involved, and the menses may continue normally thereafter, though this is not by any means always the case. One hopes with treatment also to relieve symptoms associated with the abnormal menstruation.

Of the two groups of patients who have the amenorrheic type of menstrual irregularity, the group in which pituitary failure is considered to be responsible responds best to treatment unless the atrophy of the genital tract has become irreversible. The best results are attained when amenorrhea has been present for less than six months and for this reason treatment should be begun early.

In cases of the exogenous type of pituitary failure, general hygienic measures, administration of thyroid extract, and cyclic administration of estrogens or of estrogens and progesterone are usually sufficient to bring about return of the menses.

In the endogenous type, and in any pituitary failure when the period of amenorrhea has been more than a year, such treatment is often not sufficient to bring about return of the menses, and low-dosage irradiation over the pituitary and ovaries is resorted to. It is best to establish a normal basal metabolic rate by administration of thyroid extract and to try cyclic administration of ovarian hormones (principally estrogens) for several months before giving irradiation. Frequently also, though the menses may have become fairly well regulated by administration of thyroid extract and estrogen, the married woman does not become pregnant and, provided her husband's fertility is normal, stimulation of the pituitary and ovaries by means of irradiation may bring about

pregnancy immediately or at least in a few months after treatment. It is most essential in such cases that administration of thyroid extract and cyclic administration of estrogen be continued through the pregnancy or early abortion may occur, for, when ovarian dysfunction has been the rule and pregnancy has occurred, early abortion is a common sequence. In recent years, since potent estrogens have been available for oral administration, some women who formerly have aborted several times have carried through a pregnancy with this therapy. In our cases in which we used irradiation before we had potent estrogens, we did not appreciate this, and several abortions did occur. Fortunately, however, several of these women seemed to have more regular periods after the abortion and became pregnant again carrying through the second time all right.

In the cases of primary ovarian dysfunction, thyroid extract is used when possible to stimulate metabolism. These women usually have a near-normal basal metabolic rate. Estrogens are given cyclically to maintain the pituitary-ovarian rhythm and to control the associated symptoms. Pelvic heat is also used at times to improve the ovarian circulation. If these measures fail, low-dosage irradiation is given over the ovaries only, as a rule. If the woman is not having hot flushes, it apparently does no harm to give irradiation over the pituitary also, though I doubt that any added benefit is gained. If the young woman is having no menses, low-dosage irradiation may be given at any time. If irregular menses are still present, the treatment is best given about the twenty-fourth day after the onset of a period. If it is effective, menstrual bleeding will ensue in four or five days and another period will occur again in twenty-eight days. It is well to wait three months to see the effect of a treatment. The treatment may then be repeated if the response has not been sufficient.

Before we had potent estrogens to give cyclically, we found that the effects of irradiation would cease after three or four months and treatment would have to be repeated. In recent years we have found that when we continued to give estrogens cyclically, once we had established a cycle or a regularity for a few months, the periods continued to occur regularly.

In cases of young married women who do not want to become pregnant, I never urge use of irradiation, for symptoms they may be complaining of usually can be otherwise relieved.

We do not know how the effect of irradiation is produced but from work done in our laboratory[2] with comparative low-dosage irradiation over rats' ovaries, it would appear to produce a congestion only, which may liberate a hormone, presumably estrin. In some way a rhythm is established, because, with irradiation alone, menses tend to be established and to occur regularly for three months at least. After that time the rhythm again becomes irregular.

Irradiation over the ovaries seems especially indicated in cases of amenorrhea thought to be due to retained corpus luteum or follicle cyst. Some gynecologists reserve low-dosage irradiation for use in these cases only. They use it when they cannot rupture such a cyst or express the corpus luteum manually. Slight nausea is often experienced after irradiation, and a few women

have temporarily lost the hair over areas where the treatment was given. These are the only side effects, and no woman to my knowledge has complained about them.

There has been much criticism of low-dosage irradiation, and especially of that centered over the pituitary, because the pituitary makes many other hormones even more vital than the gonadotropic hormones, and interference with the production and secretion of these is feared. No case in point has been reported to my knowledge.

In low-dosage irradiation for primary ovarian failure, I have not noticed any added value in treating the pituitary, but neither have there been any ill effects if hot flushes were not being experienced. The only questionable ill effects may have been in the cases of sterility and normal menses that I have mentioned.

In cases of amenorrhea of more than one year's duration, if only one method of treatment were available, I would prefer low-dosage irradiation. It has proved to be the best single method of therapy in such cases. Combined therapy has been somewhat more effective; that is, when necessary, giving thyroid extract enough to raise the basal metabolic rate to –3 per cent and holding it there, and then administering ovarian hormones, particularly the estrogenic, cyclically for three months at least before irradiation, again after treatment, and on through a pregnancy, if one ensues.

I wish to acknowledge the assistance of consultants in the Section on Therapeutic Radiology of the Mayo Clinic in this study.

References

1. Rubin, I. C.: Am. J. Obst. & Gynec. **12**: 76, 1926.
2. Drips, Della G., and Ford, Frances A.: Surg., Gynec. & Obst. **55**: 596, 1932.

FEAR, AN IMPORTANT ETIOLOGICAL FACTOR IN OBSTETRIC PROBLEMS*

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IN SPITE of the fact that any ten-minute cloakroom discussion among colleagues in the specialty of obstetrics and gynecology includes mention of the vagaries of the mind and emotions of their patients, there has been no resultant study of these factors from the obstetric viewpoint. A beginning in this direction was made several years ago when the professor of obstetrics in one of our large midwestern medical schools sent one of his residents to an eastern medical school for one year's intensive study of psychiatry, but, in so far as I know, this plan has not been continued.

Most of the literature on the subject is entirely from the psychiatric or psychoanalytic approach, written and studied by psychiatrists or analysts who do not have the opportunity to see the actual working out of their theories at the bedside in the maternity hospital. The obstetrician, on the other hand, does not read the psychiatric literature and would have difficulty understanding it, if he did the reading, because of his lack of training in basic psychiatry. The result, in the main, is lack of sympathy between the specialties and inadequate understanding by the obstetrician, which makes his work more difficult for him and for his patients.

In his inaugural address as president of the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons in September, 1944, Dr. Willard R. Cooke[1] took notice of this lack of correlation between the physical and emotional problems of women. While he did not attempt to relate basic psychological facts to clinical obstetric entities he did rationalize some of the less well understood peculiarities of female psychology, and went on to say that "ninety-five per cent of the severity of human suffering is mental; a great deal of the symptomatology encountered in the practice of gynecics is of purely mental origin."

The Mental Hygiene movement which began forty years ago with the express purpose of improving the care of mentally sick patients has shown a change in direction of purpose, with much more emphasis now being placed on prophylaxis and prevention. This naturally focuses attention on causes, and we are told that most adult psychoneuroses have their origin in childhood, with particular emphasis that, in the first two years of life, the causal anlage of full-blown adult emotional difficulties is laid down. Since the most important interpersonal relationship in this period of growth is the maternal-infant relationship, is it not axiomatic that, if we have an insecure, fearful, uninformed mother, the infant is bound to be affected? And is it not true also that, if the mother

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is in a chronic state of anxiety in the early period of a baby's formative years, it is very likely that the mother's state of mind must have antedated and continued throughout the period of gestation? Ignorance breeds fear and fear is the basis for chronic insecurity and an anxiety state which leads to disrupted emotional life. It is impossible to refer all harassed patients to psychiatric consultants, since there are too few psychiatrists and the added expense is often prohibitive. It is also impossible for all obstetricians to have any sort of didactic psychiatric training, and it is certainly dangerous for an untrained man to dabble with quasianalytical psychotherapeutic techniques. However, it is not too much to ask even the busiest obstetrician to make an effort to know his patients well enough to recognize the fertile soil in which seeds of anxiety have been sown and root them out or expose them at least to the fires of sympathetic understanding. An obstetrician cannot practice psychiatry, but every time he erases a fear from his patient's mind he is doing an excellent job of psychotherapy.

Much has been written of the emotional problems of the menarche and the menopause, with suggestions regarding their attempted solution in clinical gynecology. Undoubtedly, psychogenic factors play a tremendous role in the causation of dysmenorrhea, functional amenorrhea, oligomenorrhea, menorrhagia, metrorrhagia, etc., in the youthful patient, on the one hand, and may be also present in the hot flashes, headaches, dizzy spells, backache, and abnormalities of flow in the patient in her fifth decade. However, in an attempt to be concise and contained, this discussion will be limited to psychogenic factors in relation to clinical obstetric problems.

To quote Cooke again: "When a woman discovers or imagines that she is pregnant, several conflicting emotions come into play. On the one hand, there is the subconscious satisfaction of the maternal instinct and frequently delight in the prospective advent of the baby. On the other hand, there is the basic subconscious pregnaphobia with its conscious exaggeration, fear of pain, fear of death, dislike of the inevitable deformity, and often hatred of the unwanted child and its father. Given such a foundation of conflict, it is only natural that the horrors of which she has heard, and of which she will certainly be plenteously informed by her female 'friends,' tend to create a psychoneurotic superstructure which is apparent in a great many cases. Tocophobia is probably responsible for most cases of motor dystocia. Fear of the unknown in labor seems to be the origin of most of the inhibitions of motor function and of the exaggeration of pain, and in fact constitutes the real difference between the primigravida and multigravida in labor."

Karen Horney[2] says that fear of death at delivery may be a conscious fear or unconscious, but that, in either case, its real origin is in the unconscious. She adds that maternal instinct as a primal urge may be counteracted by hostility impulses against the child which may play an important part in hyperemesis, premature delivery, and depressions after delivery.

J. Whitridge Williams[3] described a patient who rapidly grew moribund without any known physical cause and in spite of all the usual types of stimulation. After eight hours of gradually growing worse, she was given a large dose of morphine which was followed by sleep, improvement in the pulse, and a rapid change for the better. In this instance Williams felt the sole cause of

the patient's collapse was an emotional one, and that in knocking out her psyche with drugs recovery was permitted. A busy surgeon is ~~not infrequently~~ confronted by a patient who informs him before necessary surgery that she is going to die. All too often she does just that, and it seems likely that it is not a case of premonition on the patient's part. It is more logical to assume that the patient is actually, though unconsciously, committing suicide.

In order to explain the causal relationships between emotional states and subjective symptoms or actual clinical problems in obstetrics, it seems wise to begin with a study of the possibility of pre-conceptional clinical entities, and of course the most common of these is infertility itself. Horney says that frigidity can be a cause of sterility as it may be based on masturbation fears. "I have damaged myself, I shall never be able to get a child." Pseudocyesis usually results from unconscious re-enforcement of the wish for a child or on the other hand a fear of the result of extramarital sexual relations. Obstetric teaching has hesitated to mention fear as a possible cause of infertility or so-called sterility, but if one is willing to add up the twos and twos of present-day psychoanalytic knowledge and obstetric facts, the resultant fours stare us in the face. In our study of clinical problems of infertility, the following facts seem fairly well proved:

1. Most women ovulate every month between the age of puberty and the menopause.
2. Ovulation occurs about fifteen days, on the average, before the beginning of a menstrual period.
3. Many patients are conscious of definite symptoms of ovulation at this time.
4. Certain tests, such as basal temperatures, vaginal smears, and differences in electrical potential, have been used to prove the time of ovulation and this corresponds to the date of the symptoms.
5. Pregnancy results most often when coitus occurs in a close time relation to ovulation.

On the psychoanalytic side, Benedek and Rubenstein[4, 5] have shown on several occasions that the patient is unconsciously aware of the time of ovulation. With the possibility of the patient's having conscious awareness of ovulation, fear of the pregnant state can so easily permit tiredness, headache, home duties, or a thousand and one excuses to prevent coitus during the twenty-four or forty-eight hours that might result in pregnancy. With unconscious fears and unconscious knowledge of ovulation, the mechanism, though a bit more insidious, is none the less effective. Almost 30 per cent of our patients who put themselves through the sterility clinics show no demonstrable cause for their difficulty and certainly some of these are childless because they are afraid. Dr. J. P. Pratt, in an unpublished lecture on Psychosomatic Gynecology before the Michigan Society of Obstetricians and Gynecologists, made the statement that he had experienced many more positive results by telling some of these patients that "nothing is wrong in any way so now all you need to do is go on home and get pregnant" than he has by the use of the huge array of biologic hormone preparations.

In my own practice I am certain that the occurrence of pregnancy in some six or eight patients the first month after a first visit, which included only a

simple physical examination, was the result of dissolution of this fear rather than any change that occurred during the examination.

Once pregnancy has begun, these same sterility patients get into a bit more trouble than the average, in the direction of miscarriage and premature birth. In fact, habitual abortion is a type of infertility, and here again we can logically reason out a possible mechanism. It is axiomatic that in the times of great disaster like fires, floods, explosions, bombardment, etc., premature birth and miscarriage are bound to occur at an increased rate among the affected population. This happens in women who have only been frightened by the cataclysm, as they need not show any physical injury. The great tension and fear in some manner stimulate the intrinsic and sympathetic nerve centers, Braxton Hicks contractions become labor pains, and the product of conception is expelled. Is it not true that fear is the same no matter what the source may be? Squier and Dunbar[6] convincingly show this effect in their report of five patients who aborted as a direct result of being told that the attending obstetrician would be on vacation when they expected to be confined. And what is true of abortion is just as factual in regard to premature labor. If a planned vacation is announced in advance, certain patients will deliver considerably before their expected date of confinement.

Fear, anxiety, frustration, any or all of them, long have been recognized as the chief factors in hypertensive clinical states. Idiopathic hypertension and the different degrees of eclampsism or pregnancy toxemia have common factors. A suggested mechanism for the production of pregnancy toxemia may be a combination of two factors.

1. The patient's own nervous system effects, fear and tension with adrenalin secretion and sympatheticotonia—angiospasm, vagus depression, increased pulse rate, and hypertension.

2. The harmful effects of overeating in the anxious, insecure patient.

In my experience, the second group of patients is quite common. Beginning with the frequent meals early in pregnancy to ward off the uneasy nauseated feelings during the first three months, the patient goes on to eat herself sick. Many patients, when cautioned about an unseemly gain in weight, report that they just can't seem to control their eating because they have a constant gnawing sensation. Siddall and Mack[7, 8] do not feel that excessive weight gain in pregnancy has much significance in predicting impending toxemia. They find that excessive gain at some period is noted in the majority of patients with late toxemia of pregnancy and was also found to occur with similar frequency in normal pregnancy. However, they did not study the incidence of toxemia in patients who have extreme weight gains. Luikart,[9] in a much larger series of patients in whom the diet and weight were carefully controlled, is convinced that a restricted diet results in a controlled weight with less danger of toxemia, less anemia, less edema, and, in his series of 1,000 cases, the fetal mortality was ⅙ that in the uncontrolled group. Luikart states that two factors control the success of his regime, namely, that the patient must understand the program and the patient must cooperate. It seems evident that these two criteria can be

stated in another way. If the physician takes the time to gain the patient's confidence and make the program clear, the patient in turn, because of the confidence and freedom from fear, has less need for the psychological stimulation and support for her unconscious yearnings and feelings of insecurity which she ordinarily deadens by frequent nibbling and overeating.

In a busy obstetrical hospital, almost every day the problem of delay in labor arises. It seems to occur in some relation to race, and very often in patients with a seemingly lower pain threshold. When we see these patients who cry out in agony and demand sedation while the contractions are weak and far apart, we have a problem which demands much of our time, considerable of our patience and sympathy, and all of our scientific interest. Why is the patient across the hall reacting so differently when many of the actual obstetric facts are so nearly alike? After all, we have always been taught that pregnancy is the biologic end point in adult female physiology. If it is physiologic, why should the process of parturition be so agonizing?

Lull and Hingson[10] describe the pain pathways from the reproductive organs to the brain and speak of the pain of childbirth as being one of the most harrowing experiences a woman can encounter. Read,[11] on the other hand, does not agree with this. Read says, "The great intensifier of stimulus interpretation is fear. This emotion, like pain, is protective, and produces through the sympathetic nervous system a state of tension within the body. Thus we have three great evils—pain, fear, and tension. It is this syndrome which is responsible for the pain of labor . . ."

Hingson agrees on the place of fear but states it in reverse. He says, "Pain can be brought to a frightful nearness through the telescope of fear. Fear can be greatly accentuated and magnified through the microscope of pain." He also suggests that there are two methods of controlling pain.

First, the anatomic approach, i.e., by blocking pain impulses at their source as in local, spinal, regional anesthesia and caudal analgesia.

Second, the encephalic approach, i.e., by obliterating pain at its site of interpretation in the central nervous system through various forms of general, intravenous, and rectal anesthesia.

"Some measure of control is afforded by obtunding the memory of pain through the use of drugs which produce amnesia or forgetfulness. The control of fear is sometimes the more difficult of the two."

Hingson controls the pain by stopping impulses at their source. Read gets the same result by the thalamic approach with the patient acquiring the ability to relax her nervous, emotional, and physical self so that the interpretation of pain stimuli in the thalamus is less rigorous. The latter method certainly is not hypnotism, but the place of suggestion in this method of handling obstetric patients must be conceded.

However, the hypnotic state with posthypnotic suggestion has been shown by Kroger et al.[12-14] to have a sphere of usefulness in gynecics. In spite of its limitations, Kroger and his associates have had very definite results in dysmenorrhea and the nausea and vomiting of pregnancy and have delivered a high percentage of their patients without memory of pain in labor. Until we have many more trained men available, most of us are prevented from following Kroger's methods.

However, Hingson also suggests that caudal block has a definite place in the treatment of hypertension in medical and obstetric cases, thrombophlebitis, Dietl's crisis, arterial emboli of the legs and peripheral angiospastic diseases.

He also states that there is no change in the force, frequency, or duration of the pattern of uterine motility under caudal analgesia. In these patients labor progresses *more rapidly* (italics are mine) than we ordinarily would expect because of the relaxation of the cervix and perineum.

I am going to suggest that most of the clinical entities Hingson has mentioned as being influenced in some measure by caudal analgesia, in addition to rigid cervix, have certain psychogenic origins, as often demonstrated by psychoanalytic approach, and that fear can be a factor in their original manifestations. I also suggest that, with caudal analgesia, he is merely breaking up the sympathetic and parasympathetic connection with the higher emotional centers, just as surely as the neurologic surgeon does with his scalpel during sympathectomy.

All of us who are connected with the problems of the delivery room recognize the strain and uncertainty of a prolonged labor, a strain not only on the attendants in the birthroom but on the expectant mother's family, to say nothing of the patient herself. The labor pains are far apart, the fetus does not descend, the cervix does not dilate and everyone is not only anxious but tired. If the patient has been without rest for a long time she is allowed to sleep by administering a sedative and in many cases, after a few hours' rest, without too much evidence of any other change having been effected, delivery proceeds to a more rapid conclusion. Many times, with frequent strong contractions, cervical dilatation seems to be at a standstill. These are the cases in which sedation in some form seems to allow the cervix to "melt away," as we also see weak irregular contractions of almost a "false labor" type change to forceful efficient ones under small doses of hypnotics.

Why should we assume that there is some uterotropic selectivity of these drugs we use? Is it not more reasonable to assume that the cause of the delay might have been emotional? If fear can cause tenesmus of the colon and bladder, can it not cause tightness or rigidity of the cervix? If fear can cause increased adrenalin secretion, sympatheticotonia with increased pulse rate and hypertensive states, why cannot a similar origin be the basis for hypertensive toxemic conditions in pregnant patients? Why should labor pains stop completely in such a high proportion of patients when they are admitted to the maternity hospital? And why should a patient have a cessation of all pain when the doctor or nurse walks in to her room preparatory to an examination? I believe this is often unadulterated fear and that as soon as acclimatization to her surroundings is complete, progress continues uninhibited.

Conclusions drawn from the material herein presented are difficult if not impossible. Until frequent case studies correlated by parallel observation between obstetricians and consultant psychiatrists are presented, it is not wise to think of proof. However, certain impressions have been gained, and these impressions are almost incontrovertible, even in the light of our present incomplete knowledge. These impressions are as follows:

1. Fear and the ultimate ramification of its effects can change the physiology of the human organism.

2. Pregnancy and labor should be physiological processes. However, because of the complete control of the reproductive system by the sympathetic and parasympathetic nerve chains, the function of reproduction is very susceptible to emotional stimuli. Fear, leading to tension, can disrupt the reproductive function in devious ways.
3. The avoidance of the effects of fear is in the hands of the obstetrician. He should first avoid increasing his patient's fears by words or deeds or by passively accepting a situation which expresses the patient's insecurity in the slightest degree.
4. The obstetrician should actually thwart the effects of fear by establishing a rapport with his patient as quickly as possible, and he should answer all questions simply and encouragingly. He should recognize his own limitations and call in the trained psychosomaticeist whenever possible.

References

1. Cooke, W. R.: Am. J. Obst. & Gynec. **49**: 457-472, 1945.
2. Horney, K.: Am. J. Obst. & Gynec. **25**: 694-704, 1933.
3. Williams, J. W.: Textbook on Obstetrics, ed. 6, New York, 1930, D. Appleton Co., pp. 1046-47.
4. Benedek, T., and Rubenstein, B. B.: Psychosomatic Medicine **1**: 245-270, 1939.
5. Benedek, T., and Rubenstein, B. B.: Psychosomatic Medicine **1**: 461-485, 1939.
6. Squier, Raymond, and Dunbar, Flanders: Psychosomatic Medicine **8**: 161-175, 1946.
7. Siddall, R. S., and Mack, H. C.: Am. J. Obst. & Gynec. **26**: 244-249, 1933.
8. Siddall, R. S., and Mack, H. C.: Am. J. Obst. & Gynec. **36**: 380-386, 1938.
9. Luikart, Ralph: Am. J. Obst. & Gynec. **52**: 428-434, 1946.
10. Lull, C. B., and Hingson, R. A.: Control of Pain in Childbirth, Philadelphia, 1944, J. B. Lippincott Co.
11. Read, Grantly Dick: Childbirth Without Fear, New York, 1943, Harper & Bros.
12. Kroger, W. S., and De Lee, S. T.: Am. J. Obst. & Gynec. **46**: 655-661, 1943.
13. Kroger, W. S., and Freed, S. C.: Am. J. Obst. & Gynec. **46**: 817-822, 1943.
14. Kroger, W. S., and De Lee, S. T.: Am. J. Obst. & Gynec. **51**: 544-52, 1946.

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SPINAL (SADDLE BLOCK) ANESTHESIA IN OBSTETRICS*

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ANALGESIA and anesthesia are important medical treatments to anyone who is in pain. The parturient woman is justified in her demand for relief from the pains of labor and of delivery if it can be given without endangering her life or the life of her baby. No doctor is justified in refusing pain relief to the woman in labor, and no doctor is justified in using analgesia and/or anesthesia to a degree which is dangerous to the life of the mother or the baby. The numerous methods of analgesia for labor would indicate that none is satisfactory. This is not true. There are several methods that the experienced obstetrician can use to give amnesia-analgesia to 85 to 95 per cent of the women in labor. Anesthesia for the delivery is a more precise procedure and depends entirely on the presence of one qualified to administer the anesthetic of choice.

The doctor must always remember that any interference with the normal course of labor—hypnotics, oxytocics, anesthetics—increases the hazards for mother and baby. Continuous caudal analgesia has been used by us in several hundred cases, but our own experience, as well as that reported in the literature, indicates that continuous caudal is not the optimum type of analgesia and anesthesia. It requires considerable skill and has potential dangers that cannot be completely eliminated. Spinal anesthesia has been used for many years, and although it, too, is potentially dangerous, it requires less skill in actual administration than does continuous caudal analgesia.

It was our purpose to determine the advantages and disadvantages of spinal (saddle block) anesthesia for the relief of pain in labor and for the delivery. We have demonstrated to our satisfaction that, with some training, the average physician can administer spinal anesthesia for relief of the pain of the late second stage and for the delivery, with a high degree of safety. In fact, this type of anesthesia is far safer than an inhalation or intravenous anesthetic administered by an inexperienced individual. We believe that the subcutaneous injection of 0.01 Gm. of morphine and 0.0005 Gm. of hyoscine without any repetition of the morphine but repeated injections of 0.0003 Gm. of hyoscine at 45 to 90 minute intervals can be used with safety by the experienced doctor for the relief of the pain of the first and early second stage of labor. Intermittent inhalations of nitrous oxide or ethylene gas and oxygen or a spinal anesthesia may be used for the second stage and for delivery. Our experience thus far

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with saddle block has led us to the conclusion that the qualified specialist, employing proper obstetric judgment and technique, may use this method of analgesia and anesthesia during the latter part of the first stage of labor as well, and may repeat the spinal injection in carefully selected cases.

The ideal regional anesthesia for labor and delivery could be imagined as a single-injection technique employing a small dose of an agent possessing a prolonged duration of effect and capable of being limited precisely to segments of the body between the umbilicus and the upper thigh.

It is probably with these factors in mind that Parmley and Adriani[1-2] first carried over into obstetrics the work of Adriani and Roman-Vega[3] on modified saddle block anesthesia using Nupercaine.

Present Study

This is a study of 719 cases of modified saddle block anesthesia carried out at the Chicago Lying-in Hospital between Jan. 5, 1947, and April 24, 1947. These cases represent 58 per cent of all patients delivered during this period of time.

All of the spinal anesthetics for six weeks were administered by three assistant residents whose only responsibility in the case was that of carrying out the saddle block procedure. They had had only the usual amount of training in anesthesia that is associated with the internship of one or more years plus varying degrees of experience in the Army or Navy. After the routine had been established and these three men were well trained, six other assistant residents and two physician anesthetists took part in the spinal anesthetic program. The training of all the doctors taking part in the study was under the close direction of one of us (G. J. A.) who has had an extensive experience with caudal and other regional anesthesia methods in association with R. A. Hingson.

A special anesthetic form was used on which all pertinent data were recorded with the exception of the drug used; which, together with the patient's name and number, was recorded on a separate sheet which was clipped to the special record form. One of us (W. J. D.) removed the separate sheet containing the name of the drug and arranged the special form sheets in groups of approximately 50 or 100, in all of which the same drug was used. When the study was completed, two of us (G. J. A. and H. D. P.) analyzed these various groups without knowing what drug was used. When all of the groups had been analyzed, the key was supplied by W. J. D. Similar groups were then combined and represent the basis for this paper. The data in Table I illustrate the results in various groups and show that the observations were properly made and the study carefully carried out since, in general, there is little difference for the various groups. On the other hand, there is enough variation to show the necessity of obtaining data from a large group of cases. This method of study increased the amount of work, and prevented any changes during the course of the work, but did permit, we believe, a most complete evaluation of spinal (saddle block) anesthesia in obstetrics.

The technique of anesthesia was demonstrated to us by Parmley, and was used throughout the study with minor modifications only in so far as drugs other than Nupercaine were involved. The majority of the injections were carried out with the patient in her labor bed, under the mattress of which had been

inserted board supports to prevent sagging. The patient was placed in a sitting position over the side of the bed, bending forward and supported by an assistant. The lower back was prepared with alcohol and a mercurial tincture. Local anesthesia infiltration of skin and deeper tissues was not carried out.

TABLE I. COMPARISON OF SOME DATA OBTAINED IN ANALYSIS OF VARIOUS "UNKNOWN" GROUPS OF PATIENTS

GROUP	PER CENT						
	A	B	C	D	E	F	G
Patients delivering after 60-120 minutes of analgesia	49	41	48	53	60	52	36
Patients requiring at least one postpartum catheterization	19	34	24	22	16	22	30
Patients with some postpartum headache	13	14	9	18	17	18	24
Patients with systolic blood pressure fall of 0-30 mm. Hg	82	78	88	83	87	84	83

Groups A-E each represent ± 100 patients in whom nupercaine was used.
Groups F-G each represent ± 60 patients in whom pontocaine was used.

Spinal puncture was made at the level of the fourth lumbar interspace. In case of difficulty at this point the third space was utilized. A short-beveled 22-gauge needle three inches in length was used in the majority of cases.

When a free flow of clear spinal fluid was obtained, a Luer Lok syringe containing the properly prepared solution (Table II) was attached to the spinal needle, aspiration of 0.1 c.c. spinal fluid carried out, and the solution injected rapidly. At the end of ten seconds the needle was removed, and at the end of thirty seconds the patient was placed flat on her back with a pillow under the head to keep the neck sharply flexed. The procedure was timed to be carried out in its entirety between contractions of the uterus, to prevent any abnormally high level or aberration of anesthesia which might result from spinal fluid turbulence coincident with contraction.

As soon as the patient was in the supine position, the following observations were made and recorded on the specially prepared form. The blood pressure was taken at least every five minutes for the first thirty minutes following the injection of the drug, and every fifteen minutes thereafter. Basal blood pressure was determined by regular observations throughout labor preceding the block, including one reading immediately before the induction of anesthesia. Observations of the maternal pulse rate and fetal heart rate were made between blood pressure readings. Oxygen and emergency drugs including ephedrine, Methedrine, Coramine, and (soluble) sodium amytal were kept immediately available. The patient was not moved or allowed to change position for twenty minutes after the injection.

All but seven of the anesthetics were completed with four drugs. These drugs with dosage and method of preparation with glucose are presented in Table II.

Buffered nupercaine (formerly percaine) in 1:200 solution, the drug used by Parmley and Adriani, was administered to 404 patients in dosage of 2.5 mg. Premixed unbuffered nupercaine (2.5 mg./c.c. in five per cent glucose) was tried in 109 instances. These two gave statistically similar results (Table I) in our hands, and have been grouped together as Drug 1 in our analyses.

Pontocaine (tetracaine) hydrochloride (Drug 2) was used in 115 cases. The dose was arbitrarily selected as 5 milligrams. By employing the 1 per cent solution of the drug, it was possible to create a technique for preparation with 10

per cent glucose which was identical to that for 1:200 nupercaine. This was deemed of importance by us in setting up a routine which would prevent accidental improper dosage.

TABLE II. PREPARATION OF ANESTHETIC AGENTS USED

DRUG	DOSE (MG.)	METHOD OF PREPARATION	TIME SITTING UP (SECONDS)
1. (a) Nupercaine (buffered) 1:200 sol.	2.5	Draw up 2 c.c. of 10% glucose, then 2 c.c. of nupercaine. Mix. Discard all but 1 c.c.	30
(b) Nupercaine (unbuffered) 2.5 mg./c.c. in 5% glucose		Draw up 1 c.c. of prepared solution. Use as such.	
2. Pontocaine 1% sol.	5	Draw up 2 c.c. 10% glucose, then 2 c.c. of pontocaine. Mix. Discard all but 1 c.c.	30
3. Novocain (Procaine) 20% sol.	50	Draw up 3 c.c. 10% glucose, then 1 c.c. of novocain. Mix. Discard all but 1 c.c.	35
4. Metycaine 10% sol.	33	Draw up 2 c.c. 10% glucose, then 1 c.c. of metycaine. Mix. Discard all but 1 c.c.	35

1. Nupercaine is alpha-butyloxycinchoninic acid diethylethylenediamide hydrochloride.
2. Pontocaine is dimethylaminoethyl-p-N-butylaminobenzoate hydrochloride.
3. Novocain (Procaine) is diethylaminoethyl p-aminobenzoate hydrochloride.
4. Metycaine is gamma-(2-methyl-piperidino)-propyl benzoate hydrochloride.

Novocain (procaine hydrochloride) (Drug 3) and Metycaine (Drug 4) were selected as shorter-acting agents to be tested under the saddle block technique. Novocain was used in 27 cases, with an arbitrary dosage unit of 50 milligrams. One part of a 20 per cent solution was combined with three parts of 10 per cent glucose. It would be possible to use a 10 per cent solution of the drug and create a method of preparation with glucose identical to that used for 1:200 nupercaine and for pontocaine, without altering the ultimate dose of the agent.

In the use of metycaine the dose was selected as 33 milligrams. Using a 10 per cent solution of the drug, one part was combined with two parts of 10 per cent glucose. The period of time the patient was allowed to sit up after the injection of novocain and metycaine was increased from thirty to thirty-five seconds after a few cases, to obtain skin levels of anesthesia more consistently at thoracic dermatome segments nine and ten. Forty-seven patients received metycaine.

Seven additional cases received monocaine formate.* The dose of this drug used was 50 mg. in crystalline form dissolved in 1 c.c. of 10 per cent glucose. The results are included in the analysis of the entire series of cases, but it was not felt proper to attempt any detailed evaluation of the drug in view of the small number of patients receiving it. The duration of effect of 50 mg. of monocaine appeared to be comparable to that of metycaine and novocain in this series. The greatest source of difficulty in the use of the drug in our few cases was the inconstant level of anesthesia obtained. There appeared to be no obvious relation of level of anesthesia to the period of time the patient remained sitting up after the spinal injection.

*2-iso-butyl amino ethyl para-amino benzoate formate.

It will be noted that the concentration of glucose in the solution injected varied with the drug used, with the exceptions of nupercaine and pontocaine, where equal parts of the drug and 10 per cent glucose were used. In each instance, however, the solution was hyperbaric in relation to spinal fluid.

In 24 of the 719 cases (3.3 per cent) there was failure to obtain anesthesia. Fourteen of those failures were converted to successful cases by repeating the tap and injection. In the remaining 10 patients the blocks were not repeated, by preference of the anesthetist or the obstetrician in charge of the case.

In our series of 709 successful anesthetics there were 346 primiparas and 363 multiparas. The ages of the patients ranged from 18 to 42 years. Complications to pregnancy existed in 117 cases. The most common of these was upper respiratory infection, occurring 43 times. Rheumatic heart disease was present in ten patients, diabetes mellitus in three, and pulmonary tuberculosis in three. Eighteen patients had preclampsia and nineteen had hypertensive toxemia. A miscellaneous group of 21 patients had syphilis, thrombophlebitis, asthma, ulcerative colitis, condylomata accuminata, scoliosis, mild degrees of psychosis, contracted pelvis, and other unrelated conditions.

It was our predetermined policy to use only single blocks in the great majority of cases. Excluding the 14 cases receiving two taps for a single successful anesthetic, there were 65 patients who received the benefits of repeat blocks, two of these having three effective injections.

This tendency to delay the block until labor was well advanced is reflected in the analysis of the series on the basis of cervical dilatation at the time of spinal injection (Fig. 1) and for hours of labor before the block (Fig. 2). It will be noted that 42 per cent of the patients had 9 or 10 cm. of cervical dilatation (by rectal examination) at the time the anesthesia was accomplished, while a total of 43 per cent were from six to eight centimeters dilated. A significant portion of the blocks performed during or near the second stage of labor were not, however, deliberately delayed to such a point. These results include many patients who entered the hospital in the final stages of labor and others who progressed under observation more rapidly than anticipated. It was our plan to institute anesthesia at 5 or 6 cm. of cervical dilatation in multiparas and near 8 cm. in primiparas. Other strict prerequisites to saddle block, as for all methods of regional anesthesia in obstetrics, should be progressive labor, an effaced cervix, fixation of the fetal head (particularly in primiparas) and no cephalopelvic disproportion.

Fig. 2 shows that 64 per cent of our patients were in labor for more than five hours before receiving a saddle block anesthetic. Obviously, premedication with some analgesic drug was desirable in most cases. Preliminary sedation was received by approximately 65 per cent of our patients. Morphine 0.01 Gm. alone or in combination with hyoscine 0.0005 Gm., was used most commonly. Demerol 0.10 Gm., alone or with hyoscine, and sodium amytal 0.2 Gm. were other agents employed frequently. It is our impression that patients premedicated with a barbiturate exhibit less apprehension and restlessness during delivery.

In Fig. 3 we have shown that 82 per cent of the patients were under saddle block anesthesia for less than 30 per cent of their labors, with a mean for the entire group of 19.4 per cent of labor.

It was found that the usual duration of complete uterine analgesia obtained from novocain (Drug 3) and metycaine (Drug 4) was from sixty to ninety minutes, with perineal anesthesia usually lasting nearly two hours. Pontocaine (Drug 2) generally gave uterine analgesia of from ninety to one hundred five minutes, and perineal anesthesia between two and two and one-half hours. In some patients the duration of effect with each drug exceeded the average.

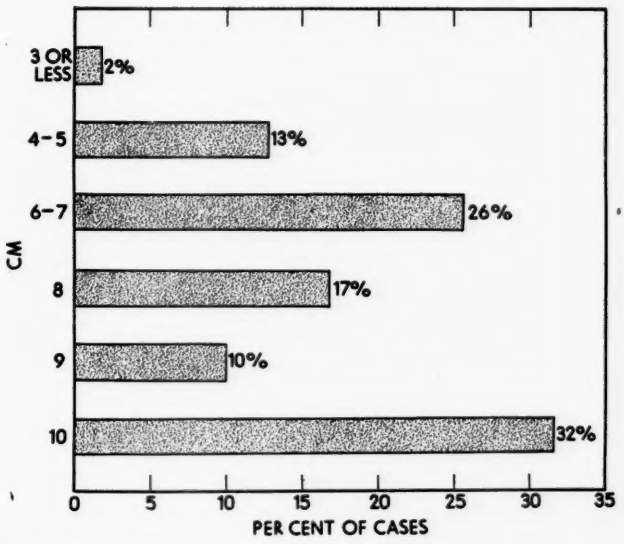

Fig. 1.—Cervical dilatation at the time of spinal injection in centimeters. By rectal examination findings, only 15 per cent of the patients were less than 6 cm. dilated at the time saddle block anesthesia was instituted, and 42 per cent were in or very near the second stage of labor.

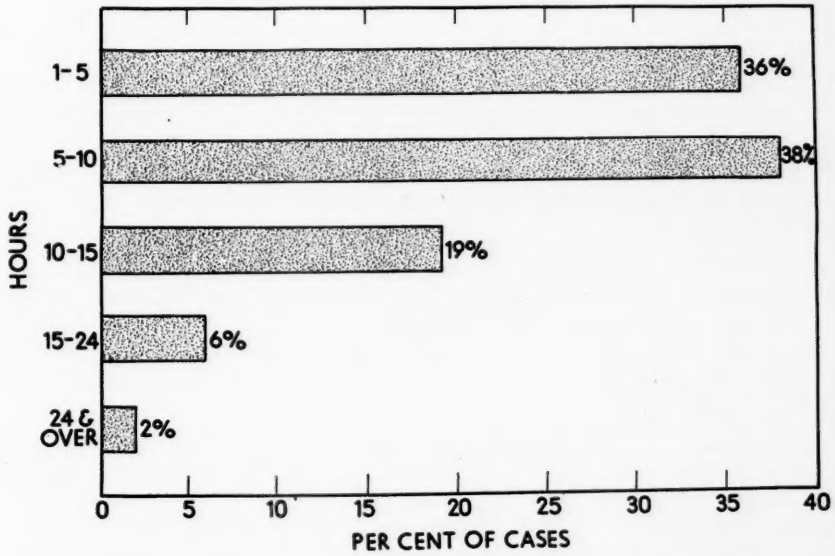

Fig. 2.—Hours of labor before spinal injection. The average patient in our series was in labor between five and ten hours before receiving the spinal injection.

We were able to observe in 100 cases the absolute duration of complete analgesia from uterine contraction pain obtained with nupercaine (Fig. 4). The mean duration was two hours and eighteen minutes. This figure is decidedly different from the average duration of three hours reported by Parmley and Adriani. Only 16 per cent of our patients in this group received three or more hours of relief with each injection of nupercaine. Where absolute duration of the perineal anesthesia was determined for the same agent, it was greater than three hours in 70 per cent of cases and greater than four hours in 42 per cent of cases.

The 65 patients who received two or three successful injections were carried under saddle block anesthesia from three hours to slightly less than nine hours when delivery was completed. Twenty patients were anesthetized less than four hours, 21 between four and five hours, and 14 between five and six hours. Nupercaine was used in the majority of these cases.

Increased incidence of failure of rotation of the occiput, delay in descent of the presenting part, and increased necessity for operative delivery procedures have been mentioned as objections to the use of regional anesthesia in obstetrics. This has been particularly evident when continuous caudal analgesia was administered early in labor. These phenomena have been thought to be the result of loss of the "bearing-down" reflex due to anesthesia of the pelvic floor and to relaxation of the pelvic sling group of muscles. We have compared the findings on vaginal examination at the time of delivery in all our patients who were managed without supplementary general anesthesia (cephalic presentations) with a control group of 2,946 patients delivered during 1944, when very little regional anesthesia was used. An insignificant increase in occiput transverse and occiput posterior positions in the saddle block group was noted.

It might be correctly assumed that any effect of regional block on the mechanism of labor would be best manifested in patients anesthetized in the first stage of labor. We have compared the types of delivery in the control and saddle block groups. The latter group has been broken down into patients anesthetized at 9 or 10 centimeters of cervical dilatation and those blocked earlier. Our comparison shows only an increase in outlet and low forceps (less marked) and a decrease in spontaneous deliveries. There were 37.6 per cent outlet forceps deliveries in the control group, 58.5 per cent in the saddle group blocked late, and 54.6 per cent in the group blocked early. In the control group 14.1 per cent of patients had low forceps deliveries, as compared to 24.0 per cent and 16.9 per cent in the respective saddle block groups.

There was no significant increase under spinal anesthesia in low forceps deliveries preceded by manual or forceps rotation, nor in midforceps procedures. All primiparas and many multiparas on our service are delivered by an outlet or prophylactic forceps with an adequate episiotomy made before the perineum has been greatly stretched by the presenting part, regardless of the type of anesthesia used.

Prolonged duration of the second stage of labor has been given as another indictment against the regional methods of anesthesia. It might be expected that the effect on the duration of the second stage would be manifested in those cases blocked at eight centimeters or less of cervical dilatation. Eighty per cent of the patients in our series who fell into this group had a second stage of less than one hour, and an additional 15 per cent of less than one and one-half hours. One patient remained in the second stage for three hours and nine minutes (negligence of resident).

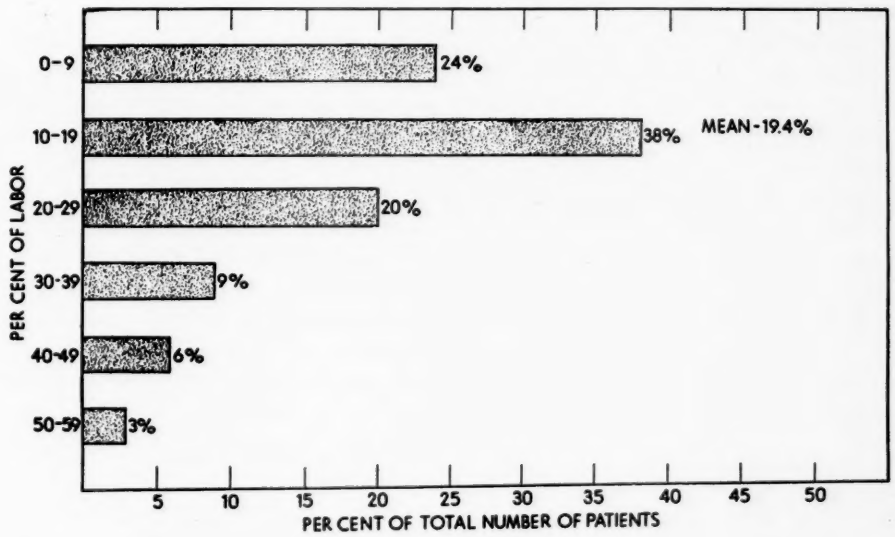

Fig. 3.—Per cent of labor under spinal (saddle block) anesthesia. Eighty-two per cent of our patients had saddle block anesthesia for less than 30 per cent of their entire labor, with a mean of 19.4 per cent of labor.

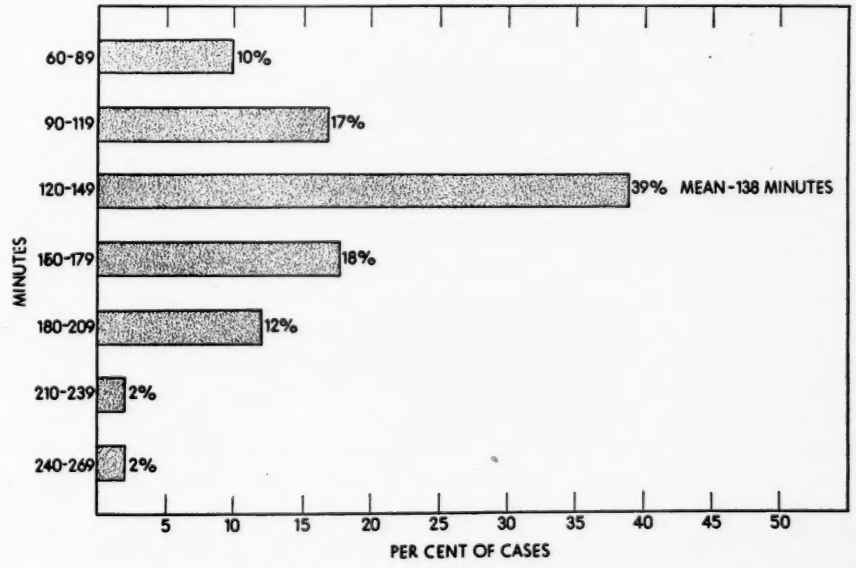

Fig. 4.—Duration of uterine analgesia to return of pain. The absolute duration of effect (uterine analgesia) of nupercaine is revealed in 100 cases who had return of contraction pain before delivery intervened.

Considering the low incidence of major operative delivery procedures necessary in our series, it cannot be said that the use of saddle block anesthesia increased significantly our operative rate. It must be emphasized, however, that we have delayed instituting anesthesia until labor was well established and we had determined the lack of significant cephalopelvic disproportion by allowing fixation of the fetal head to take place before carrying out the spinal injection.

When these factors are ignored or judged incorrectly, progress of labor may be delayed unduly and major operative intervention may become necessary.

The irritability of the uterine musculature, resulting from lack of motor paralysis in the active segment, renders extensive manipulative procedures within the uterus difficult under spinal and caudal anesthesia. We have not attempted version and extraction in any case of single pregnancy. In eight sets of twins delivered under unsupplemented saddle block anesthesia, version and extraction on the second infant was accomplished without difficulty five times. The procedure must involve working between uterine contractions, care to prevent early rupture of the membranes, and gentleness of manipulation within the cavity of the uterus. In one case where delay in attempting the version followed rupture of the membranes, the uterus contracted around the second twin, necessitating general anesthesia for relaxation.

There were twelve cases of single breech and seven cases of double breech position in our series. Breech extraction was performed fifteen times and delivery with manual aid on four occasions. We have found the extreme relaxation of the lower birth canal and of the lower uterine segment of great value in breaking up single-breech positions high in the pelvis. Again, care must be taken to work between uterine contractions and to avoid vigorous manipulation of the active upper segment of the uterus.

The management of the third stage of labor in cases delivered under gas anesthesia has included intravenous injection of 0.2 mg. Ergotrate at the time of delivery of the anterior shoulder, with a pause of thirty seconds after injection before extraction of the remainder of the body (Davis and Boynton[4]). Recently Dieckmann[5] has shown that slow delivery of the baby (three and one-fourth minutes in primiparas) is the important factor in decreasing the time of the third stage, while the use of Ergotrate or posterior pituitary (one unit in one c.c.) serves to control the blood loss during the placental stage.

We have managed the third stage with and without the use of an oxytocic drug during the second stage. We have felt that the lack of motor anesthesia in the muscular portion of the uterus would enhance contractility and thereby hasten separation of the placenta while serving to control blood loss (Vaux and Mitchell).[6] With no oxytocic in the second stage 89 per cent of the placentas were delivered in six minutes or less, and 58 per cent in three minutes or less. It is difficult to prevent the house staff from hurrying the delivery of the baby once the head is born.

Where ergotrate was injected intravenously with the delivery of the anterior or posterior shoulder a somewhat greater percentage of patients had a third stage of three minutes or less in duration, but there was no difference in the total percentage of patients in the two groups having a third stage of six minutes or less. Among the patients receiving ergotrate in the second stage there was evidenced a greater percentage of prolonged third stages as well as a marked increase in the number of manual removals of the placenta. This is accounted for by the tendency of the irritable uterus to contract rapidly under the influence of the oxytocic, with a trapping of the separated placenta in the

contractile portion of the uterus. Manipulation of the uterus through the abdominal wall before complete separation often results in retention of the placenta though no oxytocic has been given.

Episiotomy blood loss has been assumed by many to be greater under regional anesthesia than under general anesthesia, due to vasodilation in the anesthetized perineum. In six well-controlled primiparas delivered by low forceps extraction, episiotomy blood loss was measured by the method described by Odell and Seski[7] of this clinic. The average rate of blood loss in the phase before delivery and in the phase of repair in these cases was not significantly different from that found by the above workers in similar patients delivered under ethylene-ether anesthesia.

Any physician who observes deliveries carried out under one of the regional methods of anesthesia cannot help but be impressed by the benefits derived by the fetus. Transplacental narcosis that is the result of general anesthetic drugs is entirely lacking. The fetus is born undrugged unless preanesthetic sedation has been excessive or injudiciously timed. In Table III we have represented the time delay in initial respiration and cry in those of our cases delivered under saddle block unsupplemented with general anesthesia, with the exception of 61 cases who received whiffs of gas only during the delivery. These are included in Table III. It can be seen that almost 95 per cent of the infants breathed spontaneously in less than one minute after delivery, which is a much higher rate than with other methods of anesthesia on our service. In only 1 per cent was respiration delayed over three minutes. The great majority of the infants took their first respiration before the entire body had been delivered.

TABLE III. DELAY IN INITIAL FETAL RESPIRATION AND CRY

TIME IN MINUTES	INITIAL RESPIRATION (%)	INITIAL CRY (%)
-1	94.5	78.5
1-3	4.5	16.5
3-5	0.2	1.9
5-9	0.4	1.5
10+	0.4	1.6

The time of the initial cry also was impressively short. Nearly 80 per cent of the infants cried in less than one minute after delivery. Of the 20 patients whose babies failed to cry in less than five minutes after birth, 12 had received morphine from one to three hours before delivery, and three others less than four hours before. Eleven of the 16 babies in this group breathed spontaneously in less than one minute. Of the remaining four babies who had not received morphine, two were of breech extraction cases and one had exhibited fetal distress before the spinal injection was given. It becomes of great importance to wipe away mucus and blood from the faces of all infants born in cephalic presentation as soon as the head crosses the perineum and to maintain a clear airway in the posterior vagina during forceps delivery of the aftercoming head in breech cases.

Six of the 709 mothers who received saddle block anesthesia with some degree of success in this series failed to leave the hospital with a living baby, an uncorrected fetal mortality rate of 0.85 per cent. Three of the six babies were stillbirths, in each of whom the diagnosis of fetal death had been made before the spinal anesthetic was administered. The condition of the fetus after delivery confirmed the accuracy of the diagnosis, giving a corrected fetal mortality of 0.42 per cent.

Summaries of the three neonatal deaths are as follows:

CASE 1.—Calculated period of gestation, thirty weeks. Weight, 1,890 grams. Respiration and cry spontaneous in less than one minute. Death on fifth day of life. Pathologic diagnosis: Resorption atelectasis, minimal pulmonary hemorrhage, jaundice.

CASE 2.—Calculated period of gestation, thirty-six weeks. Weight 2,905 grams. Respiration spontaneous immediately. Death one and one-half hours after birth. Pathologic diagnosis: Congenital urethral obstruction with massive ureteral and renal dilatation.

CASE 3.—Calculated period of gestation forty weeks. Weight 4,755 grams. Outlet forceps delivery. Moderate shoulder dystocia. Two loops of cord around neck. Respiration and cry spontaneous under one minute. Sudden cyanosis and death seven hours after birth. Pathologic diagnosis: Beginning pneumonia.

Maternal complications attributable to the anesthesia were of no serious significance. An alleged tendency for the development of abnormally high levels of anesthesia has been pointed out in the past as the principal hazard of spinal in pregnant women. This has been minimized today by development of more precise techniques, increased knowledge of the physiology of spinal anesthesia, and the use of small doses of anesthetic agents.

With the technique as first described by Parmley and Adriani and used by us without modification, 94 per cent of our patients obtained skin levels of anesthesia at either thoracic ninth or tenth segment. An equal number of patients were anesthetized to each of the two levels, and an additional 3 per cent had a level at thoracic eight. Five patients received anesthesia to thoracic five, and there were no anesthesia levels above that point. With this consistency of level not only were the potential dangers of high spinal anesthesia to mother and fetus minimized greatly, but there was very little evidence of slowing of labor due to paralysis of motor nerve elements to the active uterine segment. These generally leave the spinal cord in sympathetic nerves at high thoracic levels.

Fig. 5 indicates the effect of the nerve block on the systolic blood pressure in nonhypertensive patients. There was no significant change in 44 per cent of cases, and a maximum fall greater than 20 mm. Hg in 26 per cent. The lowest blood pressure recorded was 60/40, but there were no symptoms or signs of complete vascular collapse in this or any other patient. In the group who had a maximum fall of greater than 20 mm. Hg, no treatment was required in 70 per cent. Six per cent were given oxygen alone, 20 per cent received 25 mg. of ephedrine or 10 mg. of methedrine intravenously, and 4 per cent had a combination of the two treatments. Symptoms included transient tachycardia in 60 per cent, nausea or vomiting in 20 per cent. There was a higher incidence of significant drops of blood pressure in patients exhibiting hypertension (140/90 or greater) before the spinal injection, but in no instance did the condition of the patient prove a source of grave concern to the anesthetist or obstetrician.

Hingson[8] states that whenever the maternal blood pressure remains below 80 mm. Hg systolic for several minutes during labor, the resting and contracting uterine tone is conceivably greater than the arterial pressure. He finds that fetal anoxia is demonstrable in almost every case where this condition is allowed to exist for five minutes or longer. The systolic blood pressure fell below 80 mm. Hg for a recordable period of time in 13.7 per cent (97 cases) of the patients receiving some anesthesia. (Hingson reported such a fall in 10 per cent of 2,457 patients receiving continuous caudal analgesia at the Philadelphia Lying-In Hospital). In our patients the fall below 80 mm. Hg was less than five minutes in duration in 51 per cent of the cases, and 10 minutes or less in

75 per cent. Fetal bradycardia below 100 beats per minute occurred in 11 instances, and all responded promptly to maternal administration of oxygen and/or the intravenous injection of a vasopressor drug. There were two other cases of temporary fetal bradycardia in our series, not associated with any significant fall in blood pressure.

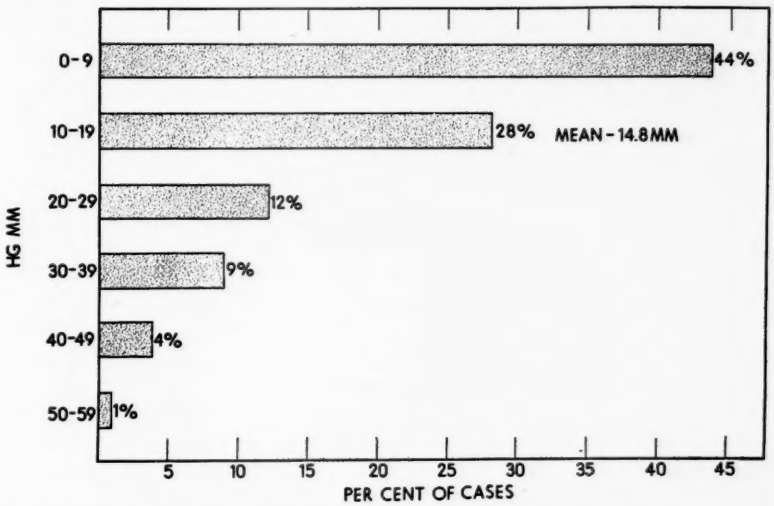

Fig. 5.—Maximum fall in systolic blood pressure in normal parturients. Excluding patients with hypertension, 26 per cent of cases had a maximum fall of systolic blood pressure of 20 mm. Hg or greater. Mean drop was 14.8 millimeters.

The incidence of postpartum catheterizations in our series was compared with a control group of 100 patients delivered with general anesthesia. An increase in the number of patients requiring only one catheterization was noticed in the saddle block cases, but little other change of significance.

Postpartum headaches in our patients proved to be a source of mild annoyance, but in no way caused us to doubt the utility of the saddle block procedure. This symptom was observed in 14.5 per cent of all patients, 10.2 per cent having "mild" headaches, 3.5 per cent "moderate," and 0.8 per cent "severe." There was no apparent difference in incidence with the various drugs used. These data were part of the information obtained by the three physicians doing most of the blocks as they made daily rounds on all patients during the entire postpartum period of hospitalization.

A headache was classified as "mild" if it did not interfere at all with the patient's activities and required no more than acetylsalicylic acid for relief. A "moderate" headache was one which required codeine or various other agents for relief and which limited in part the patient's activity for one or more days. Headaches not relieved completely by any of the usual forms of medications recommended for postspinal cephalalgia and which kept the patient more or less flat in bed were classified as "severe." There were no intractable headaches in our series. The typical time of onset was 36 to 48 hours post partum, with duration gnerally 48 to 72 hours. Four patients were confined to their beds for as long as five days by their headaches. It was our policy neither to restrict the patient's activity or position immediately after delivery under saddle block, nor to interfere with the general hospital regime of progressive early ambulation. This routinely begins with the patient sitting up in a chair after twenty-four hours following delivery have elapsed.

Early postspinal neurologic sequelae were not noted in this series, and to date (February, 1948) no late complications have been reported.

One maternal death occurred in this series. A 36-year-old para ii who had an uneventful saddle block anesthetic for one hour and thirty minutes died suddenly twenty-two hours after an outlet forceps delivery. She had had superficial thrombophlebitis ante partum. A massive embolism to the right heart was found at necropsy, and no contributing factors from the anesthetic were noted.

The average postpartum morbidity in the hospital is 8.3 per cent. The morbidity in the saddle block group was 2.6 per cent; however, this figure is based on only 719 cases, while the hospital figure is the average for some twelve years. It is of significance that no patient developed pneumonitis, an important cause of postpartum morbidity in winter months when general anesthesia is used for delivery.

Supplementary inhalation anesthesia was used in 96 or 13.5 per cent of the 709 patients in our series who received some benefit from the spinal injection. In 28 cases the saddle block was allowed to wear off completely and was not repeated. Fifty-seven patients came to delivery with waning spinal anesthesia or complained of severe pain during attempted delivery and these were given some supplementary gas. In 11 cases a general anesthetic of some degree was used by preference of the obstetrician, in the face of apparently adequate spinal anesthesia. The general anesthesia supplement amounted to whiffs of gas or a light ethylene-oxygen mixture for analgesia during the delivery procedure alone in 61 cases. Many of these patients had not received any (or adequate) preliminary sedation, and were extremely apprehensive during delivery. In this group the episiotomy repair was done without gas anesthesia. Complete general anesthesia for delivery and repair was given to 31 patients, and some supplement for all or part of the repair alone to four patients.

In the group of patients who received no supplementary analgesia, 84 per cent noted no discomfort during delivery or repair, 14 per cent complained of mild discomfort, and 2 per cent were moderately uncomfortable. When discomfort was present, it was generally in the form of marked pressure in the low back or in the perineum during delivery of head and shoulders of the fetus. Occasionally there was pain in the upper abdomen during forceps traction.

Elimination of grossly unstable individuals and the judicious use of preanesthetic medication will do much to reduce the incidence of partially unsuccessful cases in any form of regional anesthesia. Preparation during the antepartum period plus reassurance of the patient during the period of delivery assist greatly toward creating a smooth anesthetic. In inadequately sedated individuals, slow intravenous injection of 0.01 Gm. morphine after clamping of the cord will relieve restlessness from discomfort in the legs during repair of the episiotomy.

In evaluating our results objectively we classified the outcome in each case as excellent, adequate, poor or failure. The result in any case was considered excellent if there was no discomfort during labor and delivery under the saddle block and no postpartum complications of any degree. The number of patients in this group amounted to 72.2 per cent of all cases. In 20 per cent the result was adequate, indicating mild discomfort with delivery and/or minor postpartum headache or urinary difficulty. There were 6.4 per cent poor results. These patients needed general anesthesia supplement because of inadequate pain relief, or they had definite difficulties in the postpartum period. Cases in which a successful block was allowed to wear off and was not repeated were not considered as poor results for this reason alone. Failure to obtain any anesthesia occurred in 1.4 per cent of cases.

Each patient's reaction to the saddle block procedure was obtained during the period of hospitalization after delivery. In 80 per cent the response was one of enthusiasm for the method. A good reaction was elicited from 13 per cent, fair from 6 per cent, and poor from 1 per cent. There was no significant difference in the responses from primiparas and multiparas as groups.

Discussion

One of the authors, W. J. D., has had an extensive experience with various types of analgesic and anesthetic drugs in parturient women. He has seen many doctors enthusiastically endorse some new drug only to give it up for something newer a year or two later. We believe that the doctor who does obstetrics must familiarize himself with one or two drugs for amnesia-analgesia, and with a general anesthetic and one or two methods of regional anesthesia for delivery. The studies of new drugs should be left to the large clinics and only accepted by the doctor when they have stood the test of several years' use and he then has learned how to administer them.

Every parturient woman must be seen at least every 30 minutes during the first stage by an experienced intern or nurse and someone must be in constant attendance during the second and placental stages. If a drug for the relief of pain is given, the intervals during the first stage between observations must be every ten to fifteen minutes or, preferably, someone with experience must be in constant attendance.

We believe that our success with spinal (saddle block) anesthesia has been due to our insistence on meticulous attention to every aspect of the procedure. The patient is evaluated as a proper candidate and her progress in labor followed carefully. At the appropriate time the technique of instituting anesthesia is carried out precisely. Particular attention is paid to exact dosage of the anesthetic agent and to timing in positioning the patient after the injection.

During the first half hour of anesthesia the physician remains with the patient. The level of anesthesia is checked closely; the maternal blood pressure and fetal heart rate are obtained at intervals of five minutes or less. Significant drops in blood pressure are treated vigorously with oxygen and/or intravenous injections of a vasopressor drug. When the patient is ready for delivery, this is done promptly. Prolongation of the second stage of labor, for the convenience of doctor or nursing staff, particularly with the presenting part resting on the perineal floor, will increase fetal mortality under any form of analgesia and anesthesia. The placental stage is carried out in such a way as to prevent blood loss.

Our experience in this large series and in 1,800 cases subsequently has convinced us that saddle block anesthesia as we have carried it out is a safe procedure in obstetrics, and one of great value to the parturient and fetus. On the other hand, misapplication of its principles, carelessness in the technic, and neglect of the anesthetized patient will result not only in poor success but in an increased fetal and maternal morbidity and mortality. This can be said for any procedure or drug used in labor and delivery. Experience is invaluable, and must be obtained cautiously.

Summary

A series of 719 consecutive cases of spinal (saddle block) anesthesia in labor and delivery have been analyzed and the results presented in detail. The procedure has been found to be safe, simple and precise; and the degree of success has been high.

The rate of operative interference in delivery was not significantly increased.

Complications attributable to the anesthetic procedure have not been a problem.

The benefits to the fetus in early spontaneous respiration have been striking.

There has been no increase in the fetal or maternal morbidity or mortality.

We wish to thank Dr. Parmley for his kindness in demonstrating to us the technique developed by Dr. Adriani and himself.

References

1. Parmley, R. T., and Adriani, J.: South. M. J. **39**: 191, 1946.
2. Parmley, R. T., and Adriani, J.: AM. J. OBST. & GYNEC. **52**: 636, 1946.
3. Adriani, J., and Roman-Vega, D. A.: Am. J. Surg. **71**: 12, 1946.
4. Davis, M. E., and Boynton, M.: AM. J. OBST. & GYNEC. **43**: 775, 1942.
5. Dieckmann, W. J., Odell, L. D., Williger, V. M., Seski, A. G., and Pottinger, R.: AM. J. OBST. & GYNEC. **54**: 415, 1947.
6. Vaux, N. W., and Mitchell, R. M.: J. A. M. A. **124**: 549, 1944.
7. Odell, L. D., and Seski, A. G.: AM. J. OBST. & GYNEC. **54**: 51, 1947.
8. Hingson, R. A., Edwards, W. B., Lull, C. B., Whitacre, F. E., and Franklin, H. C.: J. A. M. A. **136**: 221, 1948.

THE USE OF THE VAGINAL SMEAR IN A GYNECOLOGIC SERVICE*

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THE vaginal smear technique was begun in 1940 at the New York Post-Graduate Medical School and Hospital, and has now become an important aid in diagnosis in the Department of Gynecology. The material for this study was accumulated by searching all hospital and clinic records from 1940 until 1947. Included also is a large number of smears from outside private patients of physicians on the hospital staff.

Problems in the field of vaginal smear diagnosis fell into three main groups: first, endocrine; second, miscellaneous; and third, malignancy. The largest number of smears was concerned with the first and third categories, while only a few were classified in the miscellaneous column.

In this series no smears were made as a routine measure. Each was made with a definite question in mind, and usually submitted with a specific request. In this way the study differs from certain others which have been published.[1-4] Negative results are as important as positive results—especially in the diagnosis of malignancy.

The study includes several thousand smears. Many women had repeated examinations, which accounts for the fact that there were more smears than patients. The only cases excluded were those in which there was an inadequate follow-up or incomplete histologic study.

It is evident that certain of the subdivisions reported in detail are numerically small, and in these instances no conclusions were drawn from the results. It was thought best to include these small groups, however, as they may represent a trend, and they do show the possibilities of the method and demonstrate some of the various uses to which it may be put.

Different staining techniques have been used. Recently the stain devised by Papanicolaou,[5] and since modified slightly by him, has replaced others to a large extent, particularly in suspected cancer. At present this clinic is endeavoring to devise a more rapid staining method, and the preliminary results are satisfactory. Smears were made of vaginal, cervical, and intrauterine fluids, but in this review they have not been segregated.

1. *Endocrine.*—Some of the items included in the endocrine classification were the menopause, primary and secondary amenorrheas, the relation of the vaginal smear to the menstrual cycle and to the endometrial biopsy, and the effect of irradiation on the smear.

*Read before the Section of Obstetrics and Gynecology, the New York Academy of Medicine, April 22, 1947.

Many patients were studied during the menopause. The smear was utilized to answer such questions as: Is the patient in the menopause? Does she have evidence of ovarian function? Is she responding to treatment? Is the treatment adequate? Particularly in women who have had a hysterectomy, such information is not easy to obtain by other methods.

There is no characteristic smear found during menopause. All varieties, from the deep atrophic to the early crowded types, are seen. An attempt was made to place menopausal smears into one of two groups, the crowded or the atrophic. Without going into too much detail, a crowded menopausal smear shows large numbers of pale-staining superficial cells with large nuclei, often arranged in plaques resembling a syncytium. An atrophic menopausal smear is characterized by large numbers of deep cells. These criteria were established by Papanicolaou.[6] When the smear was not typical of either of these two patterns, it was placed in the one it most resembled.

Seventy-six menopausal women were studied. In 55 the menopause was physiologic, and in 21 it followed surgery or irradiation. The two latter were designated as surgical menopause. In order to find out if the vaginal smear showed menopausal changes in women who were clinically diagnosed as menopausal, Fig. 1 was prepared. This shows that approximately four-fifths of the smears agreed with the clinical diagnosis. Inaccurate clinical diagnoses were responsible for some of the lack of agreement. There was no significant difference in this regard between natural and surgical menopause.

It then semed desirable to find out whether or not there was any difference in the character of the smear depending on the type of the menopause, and Fig. 2 illustrates the findings. This shows cases of both surgical and natural menopause, and the percentage of crowded and atrophic smears. While it is apparent that the crowded type predominates in both, the atrophic type is 10 per cent more frequent in the surgical menopause. It was thought that the more severe the menopause seemed clinically, the more the smear tended to be atrophic. It was anitcipated that the sudden and almost complete cessation of ovarian function caused by surgery might result in a more marked effect on the smear, and this actually occurred. Furthermore, the effect of estrogenic therapy on an atrophic menopause often made the smear crowded before it became either cornified or follicular. On the other hand, a crowded smear was never converted into an atrophic type as the result of such treatment. If these facts were correct, they should be confirmed by a study of the type of smear as contrasted with the duration of the menopause. Fig. 3 was prepared with this in mind. This shows, in this series, that there is a definite difference in the character of the smear depending on the duration of the menopause. An arbitrary time limit of eighteen months was chosen. Before this time about two-thirds were crowded, while after this period about three-fifths showed atrophy. The effect on both patient and smear of various types of medication was investigated, but the results were not included as it was thought they might entail too much detail for such a general discussion. They will be published later in another paper. The crowded menopausal type of smear was changed more quickly and uniformly into a cornified smear than was the atrophic type. Frequently, a patient's clinical symptoms cleared up before there was any alteration in the smear. Also, when treatment was stopped, symptoms tended to recur before there was any regression in the smear. This "lag" was observed in many cases, varied from one to eight weeks in duration, and must be considered in evaluating the effect of treatment.

In some of the primary and secondary amenorrheas, low dosage irradiation to the pituitary and ovaries was given, but opportunity to study the effect of this modality on the vaginal smears was afforded in only six cases. They are

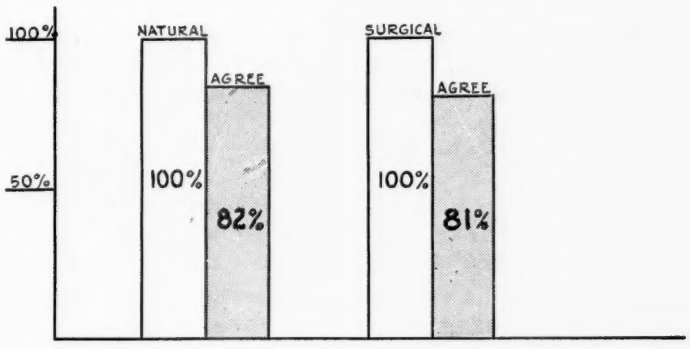

Fig. 1.—Menopause; agreement with smear.

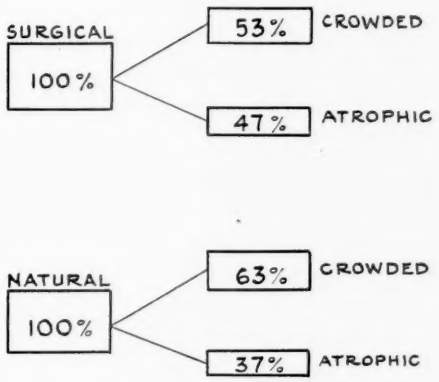

Fig. 2.—Menopause; smears which agree with diagnosis.

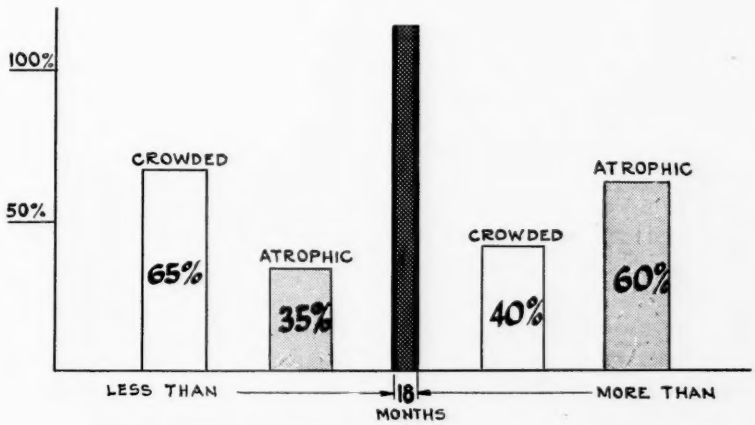

Fig. 3.—Menopause; character of smear and duration.

reported in Fig. 4, merely as an illustration of one of the phases to which this method may be applied, and no conclusions were justified.

Fig. 4 shows the results in these six cases. Five were secondary amenorrheas of various durations, and one was a primary amenorrhea. In the one case of primary amenorrhea, smears before and after therapy showed no change. No change was seen in two of the secondary amenorrheas. In another, charted as a "poor response," the smear, which was menopausal before treatment, changed to the type often seen in a secondary amenorrhea. In only two instances was a good response noted. One smear which was typical of secondary amenorrhea changed to that of a normal cycle. The sixth patient also established a normal cyclic smear and she soon became pregnant.

In a large number of instances a single smear was taken to find out whether or not it agreed with the menstrual cycle. Papanicolaou's criteria[6] were used. The type and date of the smear were checked against the known dates of the menstrual cycle. Questions asked were: Is this a normal menstruation? Has the patient ovulated? Is the follicular phase normal? Is the luteal phase normal? Is the patient going to menstruate? It at once becomes obvious that a single smear cannot answer all of these questions. A number of complete cycles was studied, and they usually did provide adequate information, but they are not included in Fig. 5 which is based on single smears only. This shows that in more than 80 per cent of cases a single smear agreed with the known phase of the menstrual cycle. Instances in which the smear failed to agree with the cycle were clinically diagnosed as follows: two were secondary amenorrheas; one, an early menopause whose symptoms cleared up under estrogenic therapy; one was a possible pregnancy on which there was no follow-up; one was a hypothyroidism with irregular menstruation; and one a case of marked obesity. These conditions were not significantly grouped, but there were many instances in which the information gained from the examination of a single smear was important.

The determination of the presence or absence of ovulation by a single smear is greatly to be desired. A previous communication[7] has detailed the experience of this clinic in this connection, but Fig. 6 brings it up to date.

At the time of endometrial biopsy to ascertain ovulation a vaginal smear was made. The biopsy was subsequently read and the smear diagnosis corroborated or disproved. It is seen in Fig. 6 that the smear correctly diagnosed this occurrence in about 90 per cent of all cases. Particular attention was given to the appearance of old cornification, grouping, and the generally dirtier appearance of the slide in deciding that ovulation had taken place. It should be stated that these changes may not actually be due to the corpus luteum hormone; at least, this has not been definitely proved. However, they accompany the appearance of this hormone quite regularly. Much more investigative work is essential to solve this problem. It is not recommended that a single smear be taken as a criterion of ovulation. It is merely pointed out that such a smear almost always gave the correct information.

Papanicolaou[8] has described a smear which is characteristic of certain of the secondary amenorrheas. It somewhat resembles the pattern of pregnancy. It is typified by the appearance of large numbers of cells from the intermediate layer. An effort was made to find out if nonmenopausal amenorrheas (exclusive of pregnancy) could be differentiated from menopausal amenorrheas by means of vaginal cytology, and Fig. 7 depicts the results.

In about two-thirds of all primary and secondary amenorrheas it was thought that a differential diagnosis from menopause could be made. All varieties of smears were seen, from deep atrophy to normal-looking pictures.

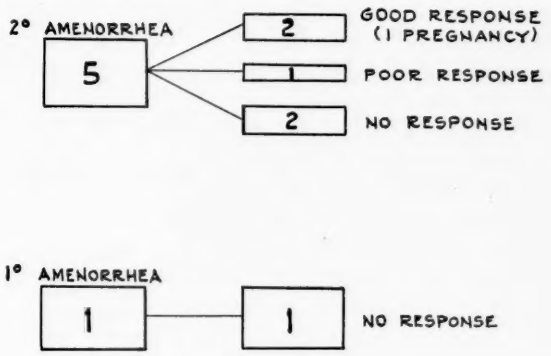

Fig. 4.—Irradiation; effect on smear.

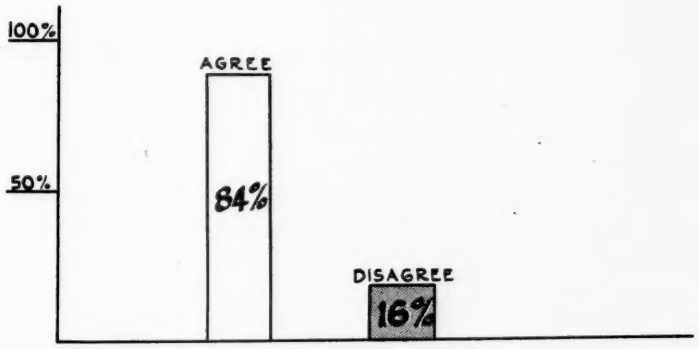

Fig. 5.—Smear and menstrual cycle.

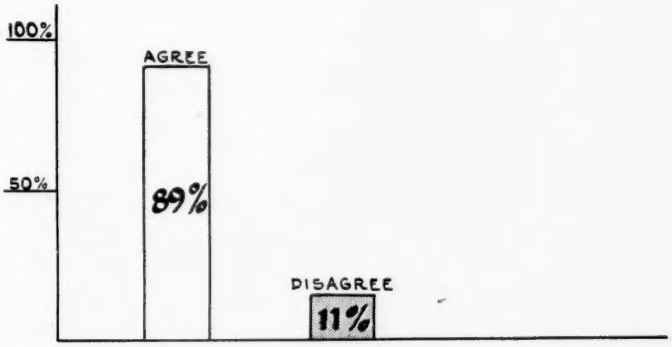

Fig. 6.—Smear and endometrial biopsy.

It was believed that this method of examination often helped to establish the prognosis. Thus, there seemed to be very little use in attempting any type of treatment for an amenorrhea when the smear showed marked atrophic changes.

In a few instances in which the clinical diagnosis was functional menorrhagia, a frequent finding was a hyperestrinemic type of smear.

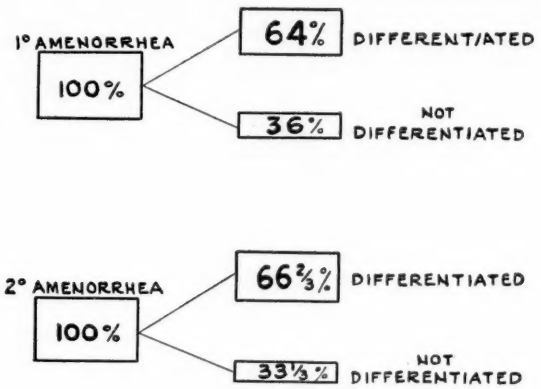

Fig. 7.—Amenorrhea (first degree and second degree); differentiated by smear from menopause.

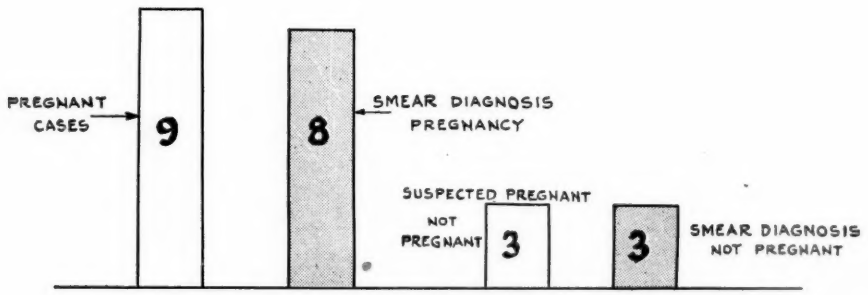

Fig. 8.—Pregnancy.

2. *Miscellaneous.*—This group is a small one, and is composed largely of cases which did not fit into either of the other two categories. It includes various types of infections, pregnancy, sterility, and certain other conditions. Some of the questions asked were: Is the patient pregnant? Has she trichomonas? What is the date of her ovulation?

In two cases of infertility of the husband, cycles were studied in the wife to determine the date of ovulation for artificial insemination. In one, nineteen inseminations were done without result; pregnancy resulted in the other from a single insemination done three days before the height of the follicular reaction. In this woman, smears taken fifteen days after conception were typically postovulatory, and not premenstrual.

Trichomonas were frequently found, often in women presenting no symptoms. In another large group, an excess of leucocytes was noted, yet the clinical findings showed no evidence of infection. Some of these may have been due to intercourse, but not all, and the appearance of large numbers of polymorphonuclear cells in otherwise normal smears requires further explanation.

The Post-Graduate Hospital has no maternity service, and relatively few women come solely for the diagnosis of pregnancy. However, this diagnosis was attempted in a small group, shown in Fig. 8.

Fig. 8 shows that 12 patients were referred for the diagnosis of pregnancy. Nine women were pregnant, and the smear made the correct diagnosis 8 times. The missed diagnosis occurred in a woman who was four weeks past her last menstrual period, and, although the smear looked premenstrual, the patient was pregnant at the time. Three women were not pregnant, and the smear showed no evidence of pregnancy. In a few postpartum smears, the appearance was characteristic. In one criminal abortion, pieces of syncytium were observed.

3. *Malignancy.*—Before going into detail of the diagnosis of malignant changes, it is necessary to state a few preliminaries. Smears were reported as positive, negative, and suspicious. The last diagnosis means that no definite malignant changes were noted, and the smear was considered negative. In such cases a request for additional smears was always made. In the statistical outline which follows, a smear was considered as in error if it was reported as suspicious and the patient really had cancer. This made for a rigid criterion of accuracy and accounted for some of the errors reported. Papanicolaou has described five types of smears in connection with malignancy diagnosis, number one being negative, number five unquestionably malignant, and the intermediate numbers being more or less suspicious. It was felt that the more uncompromising classification used in this study might prove an even more exacting test of the accuracy of the method. Suspicious smears were relatively few in number. At this point it should again be re-emphasized that these women were not referred for routine examination. Each was either a suspected carcinoma or definitely diagnosed as such. A few unsuspected malignancies were encountered while examining smears for other changes, but vaginal smears were not used in this series as a screening procedure, but rather as a means of diagnosis.

No attempt has been made to relate the specific grade of carcinoma to the smears. Except in general terms the type of cancer has not been correlated with the smear, as it was felt that this would involve too much detail in such a paper as this. Neither has the time element of the diagnosis by smear been charted in relation to the time of the histologic diagnosis. The smear diagnosis was nearly always made before the tissue diagnosis.

Occasionally, a squamous-cell carcinoma was diagnosed as adenocarcinoma, and vice versa. Except to mention such instances, they have not been included as mistakes, for it was felt that a confirmed diagnosis of cancer was sufficiently correct.

Generally only one question was asked: Does the patient have cancer? Recurrences after treatment were sometimes found. At times the diagnosis of malignancy has been by somewhat oblique means. One woman, with a solid tumor of the ovary, ascites, and hydrothorax was thought to have a possible Meigs' syndrome. Vaginal smears were negative, but smears from the chest fluid showed adenocarcinoma; at operation bilateral ovarian adenocarcinoma and carcinomatosis were found.

Changes following radiation therapy for carcinoma have as yet been very incompletely studied, but recent work from Boston[9] tends to show that such changes may be of prognostic significance. Fluid from ovarian cysts has been investigated, but not thoroughly. Malignant cells in these fluids do not look as they do in the vaginal fluid, and it was felt that this means of diagnosis was of little value.

After discarding those cases incompletely followed and those in which inadequate tissue studies were made, there were 112 women who had cancer or in

whom the diagnosis was suspected. The results of the smear examination in this series is shown in Fig. 9.

In the entire group the smear diagnosis was incorrect in 11, making its accuracy 90 per cent. If the basis of comparison is a positive histologic diagnosis of malignancy, the smear diagnosis was accurate in 89 per cent.

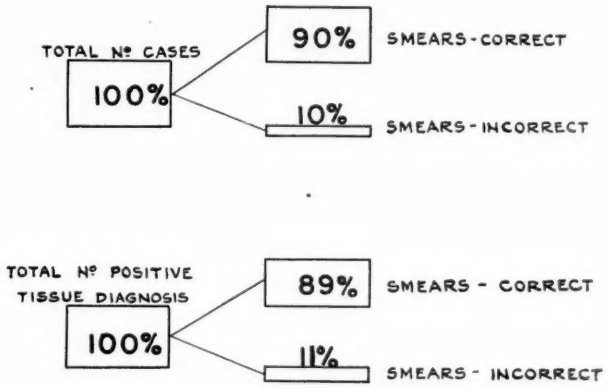

Fig. 9.—Malignancy; diagnosis by smear.

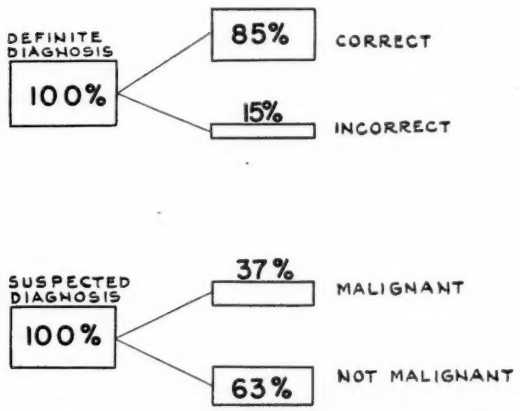

Fig. 10.—Malignancy; diagnosis clinically.

It is of special interest to scrutinize the wrong diagnoses. Seven of the 11 mistakes were false positives (6 per cent); of these, 3 were incorrectly called squamous-cell carcinoma, and 4 adenocarcinoma. Four of the 11 mistakes were false negatives (4 per cent); of these, 2 were reported as suspicious and turned out to be a squamous-cell carcinoma and an adenoacanthoma. The last 2 proved to be a squamous-cell carcinoma and a leimyosarcoma, and both were reported as negative. Another case of leiomyosarcoma was correctly diagnosed by smear.

Two instances of adenocarcinoma were diagnosed squamous cell, and two squamous-cell tumors as adenocarcinomas. Two cases of adenoma malignum were correctly diagnosed. It appears that less difficulty was encountered in this series with the diagnosis of adenocarcinoma than with squamous-cell carcinoma, which is contrary to the usual experience. In this group all cases in which the tissue diagnosis was positive for adenocarcinoma showed malignant cells in the vaginal fluid.

Frequently a definite clinical diagnosis was made. At other times the examining physician made some such note as "rule out Ca," or "possible malignancy." Fig. 10 shows the accuracy of these diagnoses.

It demonstrates that the doctor was correct in 51 (85 per cent) when he made a definite diagnosis. In the 52 instances in which he suspected the possibility of malignancy but did not definitely diagnose it, the patient was found to have carcinoma in 19 (37 per cent). It is thus seen that the diagnosis by smear corresponds very favorably to clinical judgment.

Discussion and Summary

It may be said in general that the information derived from the vaginal smear technique is a distinct addition to our diagnostic resources. It is confidently expected that its use will be more universal as time goes on. It is not suggested that it supplant the well-established diagnostic methods such as physical examination, biopsy, and biologic hormonal assays and tests, but it is suggested that vaginal smears be used as complementary to the others, and that a proper amount of credence be placed in their interpretation. There is always danger in relying too much on laboratory tests and this applies equally to vaginal smears. It is easy to accept a negative diagnosis of malignancy and then fail to carry out the other tests which will prove or disprove it.

No method is of more than passing interest if only a few men can learn to interpret it. Unquestionably, some time must be spent in learning the normal vaginal cytology, for it is by this means alone that abnormal cells and patterns may be recognized. At the New York Post-Graduate Medical School the method is taught to matriculates and they usually become proficient in smear diagnosis at the end of their course. This series represents the individual interpretation of four doctors, all of them practicing clinicians, and none spending more than a few hours at a time with the actual study of slides. This is one factor which may be responsible for the 10 per cent of errors in the diagnosis of malignancy, most of which were made during the early years of this work.

Many problems remain to be studied, and they will be more readily solved by improvement in staining techniques, both as regards simplicity and specificity. A simple, quick, and reliable office technique for staining vaginal smears is needed. Some have been described[10] but they are not yet entirely satisfactory.

As the hormonal aspects of gynecology assume greater importance, and as less reliance is placed on the curette, diagnosis by cytologic means becomes more significant. Some problems which immediately suggest themselves are: the description of a change in the smear which would be diagnostic of ovulation; further work on early pregnancy; and, possibly most important, the attempt to find a smear pattern indicative of a premalignant change.[11] When carcinoma is present, there is very little difficulty in finding it in the smears. At times this method seems to provide the only means—short of major surgery—by which cancer of the female genitals may be recognized. A few cases have been described in which borderline changes were noted in the smear, and in which the patient has developed leucoplakia and squamous metaplasia.[12] It would seem that every effort should be expended in this direction. The implications of such a

discovery would indeed be of the utmost importance, for, lacking knowledge at present of the cause of cancer, its early diagnosis is paramount.

The results of seven years' experience with the vaginal smear technique as used in the conduct of a gynecologic service have been presented. Types of clinical problems which the smear may help to solve have been discussed. Correlation has been detailed throughout with the clinical findings. Endocrine disorders, miscellaneous conditions, and malignant disease were studied. A short dissertation on some of the future problems incidental to continued use of this method has been given. The great importance of finding a method to diagnose premalignant changes was stressed.

Conclusions

1. Diagnosis by vaginal smears represents a substantial increase in gynecologic knowledge.

2. The technique is particularly useful in evaluating endocrine disorders in women.

3. The diagnosis of malignancy of the female genitals can be made in a high percentage of cases and the method should be more widely used for this purpose.

4. All efforts should be directed toward an attempt to establish a smear criterion of premalignant change.

References

1. Papanicolaou, G. N., and Traut, H. F.: Diagnosis of Uterine Cancer by the Vaginal Smear, New York, 1943, The Commonwealth Fund.
2. Ayre, J. E.: Am. J. Obst. & Gynec. **51**: 743, 1946.
3. Meigs, J. V., Graham, R. M., Fremont-Smith, M., Janzen, L., and Nelson, C. B.: Surg., Gynec. & Obst. **81**: 337, 1945.
4. Jones, C. A., Neustaedter, T., and Mackenzie, L. L.: Am. J. Obst. & Gynec. **49**: 159, 1945.
5. Papanicolaou, G. N.: Science **95**: 438, 1942.
6. Papanicolaou, G. N.: Am. J. Anat. **52**: 519, 1933 (suppl.).
7. Neustaedter, T., and Mackenzie, L. L.: Am. J. Obst. & Gynec. **47**: 81, 1944.
8. Papanicolaou, G. N., and Shorr, E.: Proc. Soc. Exper. Biol. & Med. **41**: 629, 1939.
9. Graham, R. M.: Surg., Gynec. & Obst. **84**: 153, 1947.
10. Shorr, E.: Science **94**: 545, 1941.
11. Ayre, J. E.: Am. J. Obst. & Gynec. **53**: 609, 1947.
12. Papanicalaou, G. N., and Traut, H. F.: Diagnosis of Uterine Cancer by the Vaginal Smear, New York, 1943, The Commonwealth Fund.

PREINVASIVE AND INVASIVE CARCINOMA OF CERVIX UTERI

Pathogenesis, Detection, Differential Diagnosis, and the Pathologic Basis for Management*

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THE term "preinvasive carcinoma" denotes a carcinoma which is confined to the natural surfaces and which does not penetrate the underlying stroma. We deprecate the use of the term "precancerous" for these lesions and believe that "precancerous" should be used to designate morbid changes which, from past experience, are known to be followed by cancer in many, but not all instances. In precancerous lesions a cancer cannot be detected, but is to be anticipated and therefore prevented, as for example vulval kraurosis and lingual leucoplakia. On the other hand, we believe that the preinvasive cancers are obviously neoplastic, and will ultimately invade unless they are eradicated.[1]

The criteria for the diagnosis of preinvasive cancer are based upon cytologic alterations from the normal, a change of functional epithelium to a vegetative type. The nuclei are larger than normal, vesicular and hyperchromatic, of irregular size, and the nuclear-cytoplasmic ratio is increased. Mitotic figures, sometimes bizarre, are readily demonstrable. Differentiation is either absent or incomplete. In the cervix uteri the preinvasive carcinomas not only involve the external surfaces, but also extend into the glands of the endocervix. This extension may be mistaken for invasion; however, careful study of several sections will minimize this error.

An invasive carcinoma is one in which the epithelium breaks the barriers of the restraining stroma and thereby gains access to vascular channels which may be permeated by neoplastic cells to undetectable distances and distributed as embolic implants to remote parts of the body.

Pathogenesis of Carcinoma of the Cervix Uteri

In a recent publication,[2] one of us (E. R. P.) with Auerbach described the pathogenesis of carcinoma of the cervix. The study of additional material has enabled us not only to corroborate, but to extend these observations.

Cervical squamous cell carcinomas usually begin in the endocervical canal at the junction of the stratified squamous and columnar epithelia. The source of these cancers is probably the endocervical basal cell[3] whose location corresponds to that of the early cancer. Three stages of cervical cancers have been described: (1) preinvasive carcinoma; (2) covert invasive carcinoma; (3) overt carcinoma.[2]

*Aided by a grant from the American Cancer Society.

The Preinvasive Carcinoma.—An incidence of 3.9 per cent of preinvasive carcinoma has been found in our laboratory from a study of serial blocks from 1,200 surgically removed cervices.[2] The proximity of this incidence to that of the incidence of recognizable cancer of the cervix implies that the majority of cancers of the cervix are preinvasive in their incipiency. From the initial focus, possibly foci, the neoplastic cells spread laterally, vertically, and into the glands. Vertical extension is usually upward, but occasionally the growing cells displace to a less extent the normal stratified squamous epithelium. Lateral extension frequently involves the entire circumference at the external os.

The average age of the forty-seven patients with preinvasive carcinoma previously reported was 36.6 years.[2] We have now observed sixteen additional cases and the average age of the entire series of sixty-three patients is 37.7 years. In addition to those cases in which the entire cervix was examined we have observed preinvasive carcinoma in sixty-six biopsies. The average age of the patients in which the diagnosis was made from biopsy is 40.8 years (Table I). The difference of three years is significant. Preinvasive cancers are usually asymptomatic, and cancer was not suspected in our series of surgically removed cervices. On the other hand, biopsies are usually performed on cervices suspected of having a neoplasm or in patients with symptoms. It is therefore possible that the biopsy was not representative of the whole neoplasm, and only included that part of the neoplasm which had remained preinvasive. It is also possible that preinvasive carcinomas may have escaped detection in material from the younger age group because the focus may have been so small as not to have been included in the specimen. We have repeatedly observed small foci of cancer which could be detected only by serial blocks. Preinvasive carcinomas can only be diagnosed microscopically, and in our series we have been unable, by gross examination, to suspect the existence of these incipient cancers.

Covert Invasive Carcinoma.—Ultimately the preinvasive carcinoma becomes invasive after a variable period of latency.[1] The invasion occurs either from a large surface of the endocervix or from a single focus. The early invasive carcinomas are not visible on vaginal examination, and are therefore denoted as covert invasive carcinomas. In addition to the series of eight cases which were reported previously,[2] we have examined four more recent cases and have discovered five in our files. The average age of these nineteen patients is 44.2 years (Table I). The extent of these tumors varied from minute foci of invasion,

TABLE I. AGE INCIDENCE OF PREINVASIVE AND COVERT CARCINOMAS

		YEARS					TOTAL	AVERAGE AGE
		20-29	30-39	40-49	50-59	60+		
Preinvasive carcinomas of cervix from hysterectomies or total cervices	No.	6	33	16	4	1	60	37.7
	Per cent	10	55	26.7	6.7	1.7		
Preinvasive carcinomas from biopsies	No.	6	30	13	5	6	60	40.8
	Per cent	10	50	21.7	8.3	10		
Covert invasive carcinomas	No.	0	5	9	2	1	17	44.2
	Per cent		29.4	52.9	11.8	5.9		

which were detected only in microscopic sections, to tumefaction of the entire cervix without, however, penetration of the vaginal surface. According to the information which we received with the specimen, the surgeon was unaware of the presence of carcinoma in sixteen instances. In three the neoplasm was judged to be sufficiently early to warrant hysterectomy, and in one of these the neoplasm was so advanced that a section of one ureter was included in the specimen.

Our belief that the covert carcinomas pass through a preinvasive phase is supported by the observation that a border of neoplastic epithelium, which is confined to the natural surfaces, is commonly observed in sections from serial blocks of the involved cervices. The difference in the average age of the two groups lends additional support. Speculation on the length of time cancerous cells might remain in situ has usually been reckoned in years,[4] and, according to our two series, this period of latency may average 6.5 years.

The Overt Cancer.—We have observed only two early carcinomas which were limited to the vaginal surface of the cervix, and we therefore conclude that the great majority of cervical cancers arise from the junctional endocervix and do not become manifest until there is definite penetration and ulceration of the vaginal surface of the cervix.

The average age of 100 consecutive patients with frank carcinoma of the cervix which was confirmed by biopsy was 49 years. It therefore appears that the majority of cancers of the cervix become obvious only after a period of time averaging five years after the onset of invasion and eleven years after incipiency. Clinical cancer of the cervix means advanced cancer.

Detection and Classification

The overt carcinomas of the cervix are readily suspected by vaginal examination and confirmed by biopsy. The covert invasive carcinoma in its late stage may also be suspected because of the firmness of the cervix and pericervical induration. The presence of ulceration of the portio, induration, and fixation are, however, signs of advanced cancer. In its early stages and sometimes even when advanced, a covert carcinoma may not be suspected. We have observed one specimen of supracervical hysterectomy in unsuspected carcinoma where the line of excision traversed the carcinoma. In several other instances the covert carcinoma was so far advanced that the condition of the patient was worsened rather than bettered by blind hysterectomy. It is therefore imperative that diagnostic biopsy of the cervix and curettage of the endocervix as well as the body of the uterus precede major surgery on the uterus.

There are no signs of preinvasive and early invasive carcinoma and, until ulceration ensues, symptoms are absent. Concentration of effort should be directed toward the detection of preinvasive carcinoma because therein lies the greatest opportunity for cure. Various investigators have demonstrated the value of the cervical and vaginal smear technic of Papanicolaou for detection of cancer,[5] however the final diagnosis usually depends upon microscopic study of biopsied material.

It is important that biopsies be selected to include the junction of the squamous and columnar epithelia, and due allowance must be made for displacement of this junction when ectropion and pseudoerosions are present. Furthermore, it should be emphasized that the existence of preinvasive carcinoma is frequently not detected by single biopsies, in fact, in our series of studies of serial blocks there were instances when only one or two of several blocks revealed cancerous epithelium. This is one probable reason for the differential age incidence of preinvasive carcinomas in the cervices from serial blocks and from biopsies (36.6 against 40.8) and between serial blocks of surgically removed cervices and our earliest and most recent material when only two blocks of cervix were routinely sectioned (36.6 against 39.6).

Because invasion frequently occurs from a single focus which may not be included in the biopsy, the cancerous epithelium would then appear to be confined to the natural surfaces. Therefore a differentiation should be made between the preinvasive and the covert invasive carcinomas. We therefore recommend the following procedures. When a biopsy of the cervix proves the presence of a preinvasive carcinoma, the endocervix should be curetted. If the

biopsy is obtained under general anesthesia, curettage of the endocervix and endometrial surface should be done at the same time, and preferably the material should be submitted to the laboratory in separate containers. If the biopsy is not performed under general anesthesia, then, after the diagnosis has been made, the patient should be subjected to a curettement before starting treatment (Figs. 1, 2, and 3). We are now hopeful of obtaining sufficient endocervical curettings at the time of the biopsy without general anesthesia, but our experience in this endeavor is limited. We are in accord with the observations of Schiller, Knight, and Meyer that the examination of endocervical scrapings is important in the detection of early cancer.[6]

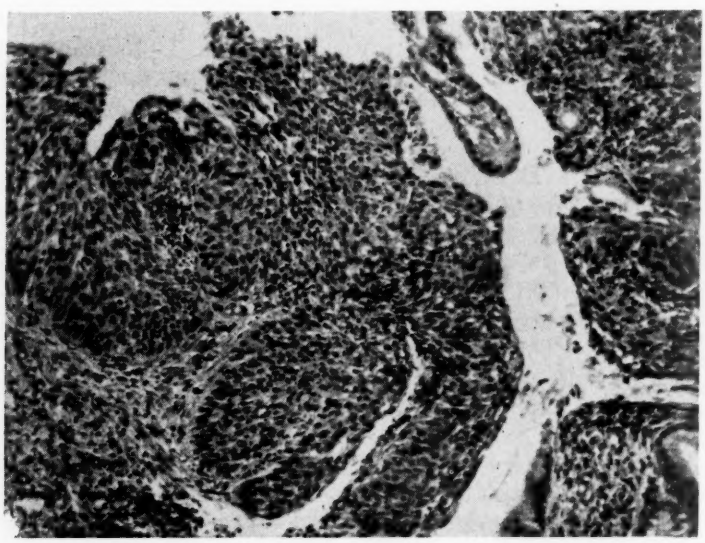

Fig. 1.—Preinvasive carcinoma found in cervical biopsy from a Negro woman, aged 29 years. Note how the carcinoma follows the natural surfaces and extends into the mouths of the glands. Endocervical curettage recommended. See Fig. 2.

Curettings should be washed momentarily in water in order to lake the blood and thus leave behind the residue of tissue. The tissue should then be transferred to normal saline or to the fixing solution. This important step enables the pathologist to select all or representative fragments of tissue. In our laboratory curettings are submitted from the operating room in a solution of normal saline. We wash the specimen in a beaker of tap water. Much of the blood is laked, the fresh clots imbibe fluid and swell so that incorporated tissue is easily removed and the mucus swells and can be readily identified. The residue of tissue is fixed in 10 per cent formaldehyde.

We have also had limited experience with the cervical smear technique of Papanicolaou[7] in detecting carcinoma in routine examinations. At the present time we have had positive films from five patients in whom a preinvasive carcinoma was detected by biopsy. In one of these patients with a positive film, a section of cervix and endocervical curettings were obtained at the same time. The three sections from the cervix did not reveal carcinoma, but in the endocervical curettings there were two slivers of recognizable cancerous epithelium. If the curetting of the endocervix is carefully performed, one should be able to determine the presence or absence of invasion, and thus distinguish between preinvasive and covert invasive carcinoma.

Choice of Treatment

It would be presumptuous in this paper to discuss the relative merits of radiation and surgery in the treatment of invasive carcinoma of the cervix. In our local department of cancer, radiation has been the treatment of choice. It is also generally recognized that the cure rate of early cancers of the cervix which are treated with radiation approaches 100 per cent.[8] We, therefore, prefer to recommend radiation for the covert invasive carcinomas and for the

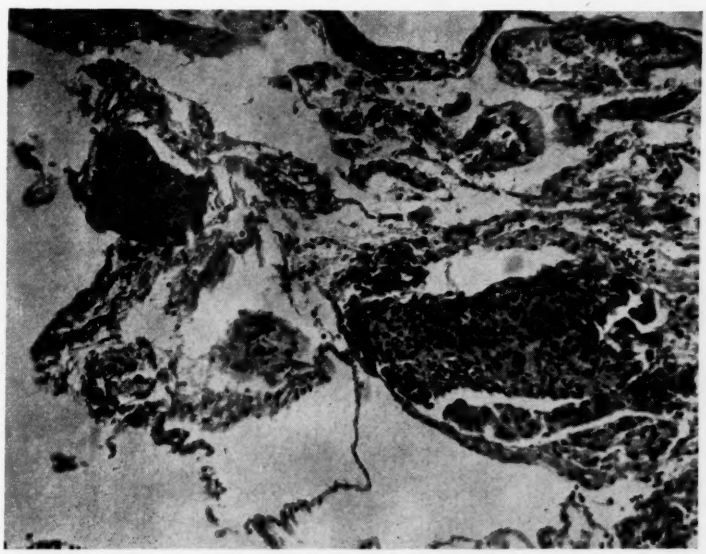

Fig. 2.—Endocervical curettings from same patient as Fig. 1. Note the sliver of cancerous epithelium, and compare with the detached fragment of metaplastic squamous epithelium. The presence of uninvolved endocervical tissue indicates lack of invasion. Hysterectomy with preservation of ovaries recommended. See Fig. 3.

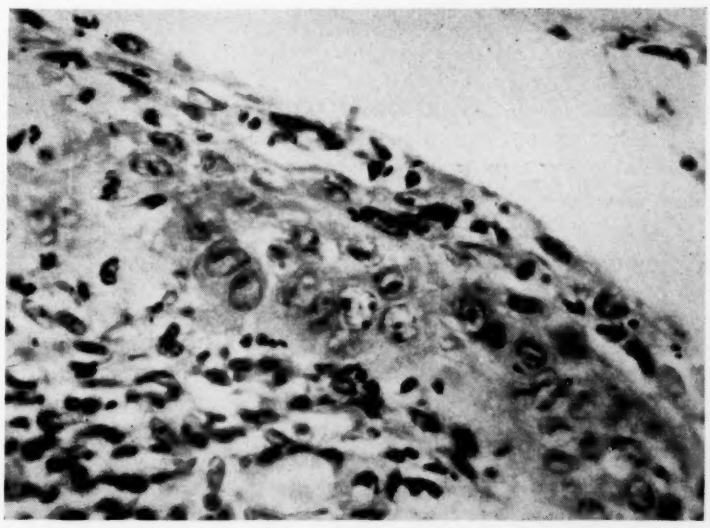

Fig. 3.—Small area of preinvasive carcinoma detected in only one of seven blocks from cervix after total hysterectomy. One ovary removed because of corpus luteum cyst.

overt carcinomas. Radiation, however, is sometimes followed by annoying and occasionally serious complications, cystitis, proctitis, endocervical strictures, pyometra and rarely fistulae. Furthermore radiation castration with its attendant symptoms frequently poses a medical problem especially in the younger age group. We now recommend total abdominal hysterectomy in cases of proved preinvasive carcinoma with preservation of the ovaries in the young. Because the average age of patients with preinvasive carcinoma is between 36.6 and 37.7 years, we deem it important to preserve the function of the ovaries.[9] It should, however, be again emphasized that this radical departure from the usual treatment should be reserved only for patients with preinvasive carcinoma, and the precautions outlined above must be adopted to determine the presence or absence of invasion. The surgeon, too, should approach each case as an abdominal exploration and, before the uterus is removed, careful palpation must determine the absence of fixation of the cervical segment or other evidence of invasion. We, therefore, issue this caution: If invasion is thought to be present the uterus should be left in place and, because radiation will be subsequently used, we recommend surgical castration at this time. This will remove immediately the hormonal activity of the ovaries and will antedate radiation castration by only a few days.

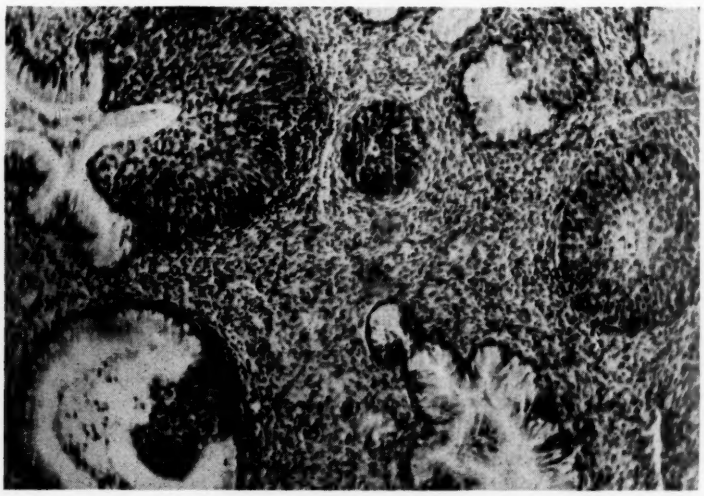

Fig. 4.—Cervical biopsy from white woman, aged 32 years. Note the presence of preinvasive cancer in several deep glands. No carcinoma was found in curettings. Subsequent total hysterectomy revealed a circumferential preinvasive carcinoma.

Measures, more conservative than hysterectomy, have been effective in the treatment of preinvasive carcinoma. We advise against cauterization and conization for two reasons, firstly, the carcinomatous epithelium is frequently found deep in the glands (Fig. 4) and, secondly, the epithelium which remains behind has been subjected to the same cancerogenic agents, whatever they may be, as the cancer-bearing area. We are also opposed to amputation of the cervix, because we have observed extension of the cancerous epithelium high up in the endocervix. In a recent case a preinvasive carcinoma was found in an amputated cervix. In the specimen from subsequent hysterectomy, seven weeks later, a preinvasive carcinoma was observed which involved the entire circumference of the cervical stump. In surgical removal of the uterus one is assured of removal of the entire area of carcinoma. In these incipient cancers there is

little probability of lymphatic extension because the stroma is not penetrated and the negligible risk of leaving the ovaries and ligaments would be counterbalanced by the preservation of ovarian activity.

Summary

The majority of squamous cell carcinomas of the cervix arise within the endocervical canal at or near the external os, therefore biopsies should include this area.

Cervical squamous cell carcinomas may be classified into three groups; preinvasive, covert invasive, and overt invasive cancer. Each group represents a stage of development over a period which averages eleven years.

Preinvasive carcinomas, the incipient cancers, are asymptomatic and can only be detected by microscopic examination.

Preinvasive carcinomas have been detected by examination of vaginal and cervical smears followed by microscopic examination of biopsies and endocervical curettings.

It is necessary to differentiate preinvasive carcinomas from covert invasive carcinomas.

The presence of a covert invasive carcinoma may not be anticipated and therefore a biopsy of the cervix and curettement of the endocervix should be a routine procedure before subtotal or total hysterectomy.

Total hysterectomy is recommended for *proved* preinvasive carcinomas, and ovariectomy is not necessarily indicated.

Appreciation is extended for Figs. 1, 2, and 3 to Lt. Col. J. M. Blumberg, U.S.A., Oliver General Hospital, Augusta, Ga.

References

1. Younge, P. A.: Arch. Path. **27**: 804, 1939.
Pemberton, F. A., and Smith, G. Van S.: Am. J. Obst. & Gynec. **17**: 165, 1929.
Smith, G. Van S., and Pemberton, F. A.: Surg., Gynec. & Obst. **59**: 1, 1934.
Stevenson, C. S., and Scipiades, E., Jr.: Surg., Gynec. & Obst. **66**: 822, 1938.
2. Pund, E. R., and Auerbach, S. H.: J. A. M. A. **131**: 960, 1946.
3. Carmichael, R., and Jeaffreson, B. L.: J. Path. & Bact. **52**: 173, 1941.
Auerbach, S. H., and Pund, E. R.: Am. J. Obst. & Gynec. **49**: 207, 1945.
TeLinde, R. W., and Galvin, G.: Am. J. Obst. & Gynec. **48**: 774, 1944.
4. Smith, G. van S., and Pemberton, F. A.: Surg., Gynec. & Obst. **59**: 1, 1934.
TeLinde, R. W., and Galvin, G.: Am. J. Obst. & Gynec. **48**: 774, 1944.
5. Papanicolaou, G. N.: J. A. M. A. **131**: 372, 1946.
Ayre, J. E.: J. South. M. A. **39**: 847, 1946.
Meigs, J. V.: J. A. M. A. **133**: 75, 1947.
6. Knight, R. Van D.: Am. J. Obst. & Gynec. **46**: 333, 1943.
Schiller, W.: Surg., Gynec. & Obst. **56**: 210, 1933.
Meyer, R.: Surg., Gynec. & Obst. **73**: 129, 1941.
7. Papanicolaou, G. N.: J. A. M. A. **131**: 372, 1946.
8. Brown, R. L., and Scarborough, J. E.: J. Med. Assoc. Georgia **36**: 385, 1947.
9. TeLinde, R. W., and Galvin, G.: Am. J. Obst. & Gynec. **48**: 774, 1944.

SPECTROSCOPIC DETECTION OF HEMATIN IN THE PERIPHERAL BLOOD

An Aid to Diagnosis of Ruptured Tubal Pregnancy

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THE term ectopic pregnancy signifies a gestation in any location outside the uterine cavity, but this discussion deals only with those occurring within the Fallopian tube. Before rupture, the diagnosis is seldom made. There is usually a history suggestive of early pregnancy, which, with irregular bleeding, makes one suspect ectopic pregnancy or threatened abortion. A tender mass located on one side of the uterus, cramplike pain, fever, and leucocytosis are usually present. After rupture, the history of early pregnancy with irregular bleeding and the occurrence of a sudden, sharp pain, followed by collapse, are characteristic of the condition. Cullen[1] finds that a bluish discoloration in the region of the umbilicus is helpful in diagnosis, but this sign is not constant. The differential diagnosis between abortion and ectopic pregnancy is of the utmost importance in the treatment of these conditions. Abortion occurs with the greatest frequency between the eighth and twelfth weeks of gestation, while tubal pregnancy may first manifest itself from the fourth to the sixth week. The bleeding in tubal pregnancy is first uterine in origin, resulting from decidual separation, which usually indicates death of the fetus in the Fallopian tube. The bleeding is usually moderate in amount and often chocolate colored. The passage of a decidual cast has been overemphasized as this is relatively rare, for usually the decidua breaks down and comes away as a part of the dark, bloody discharge. The bleeding in uterine abortion is often quite profuse and bright red in color.

In tubal gestation, the pain is usually stabbing in character, rarely colicky, and often referred to the affected side. It may be associated with a feeling of faintness or vomiting, as the result of peritoneal irritation. The pain in abortion is cramplike and rhythmical, resembling menstrual cramps. On examination in cases of ectopic pregnancy, an adnexal mass may be felt on one side of the uterus, which is semifluctuant. If there has been free bleeding in the cul-de-sac, on palpation one will feel a soft, boggy mass, which is usually tender. The uterus will be slightly enlarged and distinctly softened. In uterine abortion, the uterus will be enlarged to a size to correspond to the period of amenorrhea, and the adnexal region will usually be found negative to palpation. The cervical os is often partially dilated. Absolute diagnosis may rest upon examination of the uterine contents, which would show chorionic villi and decidua,

in the case of intrauterine gestation, but only decidua in the case of ectopic pregnancy. Puncture of the cul-de-sac or colpotomy is a frequent aid in diagnosis. In arriving at a diagnosis, the Aschheim-Zondek or Friedman test is of value only when it is positive. If it is negative, however, the possibility of ectopic gestation is not ruled out. The hormonal test becomes negative following the death of the ovum, and the separation of chorionic tissue from the tubal wall. Moreover, a positive test does not rule out the possibility of an intrauterine gestation.

Spectroscopic Detection of Hematin in the Peripheral Blood

When one surveys the various reports in the literature concerning the diagnosis and treatment of ectopic pregnancy, the results are found to be uniformly good. After supporting blood volume, the treatment of ectopic pregnancy, whether ruptured or not, is always surgical. It is common to report success in the treatment of this condition, but it is rare, indeed, to find a report showing the number of operations performed when the diagnosis was in error.

In these situations, pelvic inflammation, with or without abscess formation, appendicitis, normal intrauterine gestation, or no changes at all may be found on operation when expecting to find ectopic pregnancy. It is clear that more accurate means of diagnosis are necessary. With this in view, we are trying to make more certain of the presence or absence of extravasated blood in the peritoneal cavity.

Often a patient is under observation because of vaginal bleeding, low abdominal pain, fever, anemia, and leucocytosis in the presence of a pelvic mass. The differential diagnosis may rest upon the possibility of a pelvic abscess, hemorrhage into a cyst, appendicitis, intrauterine gestation with pelvic inflammation, or ectopic pregnancy with bleeding into the abdominal cavity. It is in such instances that additional aids in diagnosis are of value. The identification of hematin in the blood is a procedure in this direction. This was suggested to us by Dr. Isadore Snapper, formerly of the Peiping Union Medical College.

The appearance of hematin in the blood stream is not specific for ectopic pregnancy. It is significant of bleeding into a body cavity. The hemoglobin released by abdominal hemorrhage hydrolizes and liberates hematin which is absorbed into the blood. The appearance of hematin is thus characteristic of hemolysis from various causes.

Schumm[2] in 1912 first devised a method of testing for hematin in the blood. The present procedure is a modification of his original work. When blood is liberated into the peritoneal cavity, clot formation takes place within a few minutes, except in abnormal blood states, such as hemophilia. Enzymes are released which bring about lysis of the clotted blood cells. When hydrolysis occurs under the influence of the enzymes, hemoglobin breaks down into its two constituents of globin and hematin. The globin is absorbed and utilized by the body as any other protein. Hematin, an iron porphyrin compound, is also absorbed into the blood stream, where it is adsorbed by the plasma proteins. It is thought that hematin is introduced into the blood by way of the lymphatic system.

Hematin may be detected by means of the spectroscope, although it gives a weak spectrum. However, the addition of a reducing agent to hematin in the presence of plasma proteins will form a reduced hemochromogen. This gives a strong spectrum consisting of two bands. A strong narrow band is located at 558 millimicrons on the spectroscope, and a fainter wide band at 527. The first band at 558 is especially characteristic.

If oxyhemoglobin is present, a narrow strong band will appear at 577 and a wider band at 545. The addition of the reducing agent transforms the oxyhemoglobin to reduced hemoglobin, which gives a wider fainter band at 555 and its usually not seen.

If oxyhemoglobin and hematin are present, the addition of the reducing agent leads to the disappearance of the two bands of oxyhemoglobin (conversion to hemoglobin with its wide faint band which has been mentioned) and to the appearance of the two bands of hemochromogen.

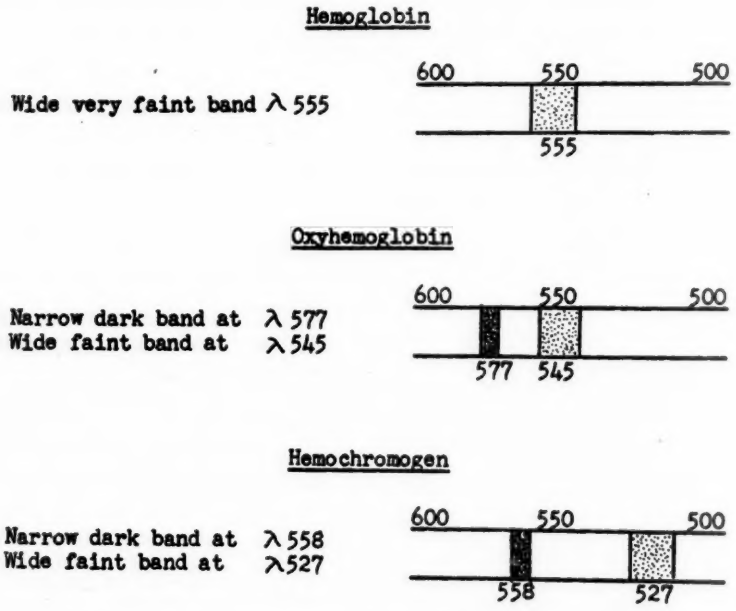

Fig. 1.—Appearance of the spectrum bands.

Technique.—Five to ten cubic centimeters of oxalated venous blood is centrifuged at 1,800 revolutions per minute for ten minutes. The supernatant clear plasma is withdrawn into a clean dry test tube and examined with the spectroscope for band visualization. A Schmidt and Haensch hand spectroscope as suggested by Wendel[3] for methemoglobin determinations was used. A few drops of a solution of ammonium sulfide[4] as the reducing agent are then added, and the spectrum re-examined for new specific band formation and disappearance of previous bands.

Fig. 1 shows the various bands of hemoglobin, oxyhemoglobin, and hemochromogen as they appear on the spectroscope. The presence of oxyhemoglobin

will depend on the amount of hemolysis that occurs when blood is drawn for testing. As can be seen, a strong band of oxyhemoglobin at 577 may be confused with a strong band of hemochromogen at 558. With the addition of the reducting substance, oxyhemoglobin is converted to reduced hemoglobin. The wide faint band of hemoglobin at 555 is not readily seen. However, an excess of oxyhemoglobin will, on conversion, form a strong reduced hemoglobin band which may mask the reduced hemochromogen spectrum. It is, therefore, essential to avoid excessive hemolysis due to trauma in drawing and handling the blood before testing.

Case Reports

The following are a few case histories to illustrate the clinical application of this test.

Case 1.—M. F. C., a 22-year-old multigravida, entered the hospital with a tentative diagnosis of incomplete abortion at ten weeks. Her symptoms dated back three weeks. She had lower abdominal pain, a 5 cm. pelvic mass, anemia, slight fever, leucocytosis, and vaginal bleeding. The test for hematin in the blood was positive. Laparotomy revealed an old ruptured right tubal pregnancy with early lithopedian changes and about 100 c.c. of old blood in the pelvic cavity.

Case 2.—M. E. W., a 32-year-old multigravida, had symptoms for nine days prior to admission suggesting incomplete abortion of fourteen weeks' duration. She had slight fever, anemia, leucocytosis, abdominal pain, a soft 7 cm. mass in the left cul-de-sac, and vaginal bleeding. Two cul-de-sac aspirations failed to reveal blood. Hematin testing was positive on two occasions. Laparotomy revealed an old ruptured right tubal pregnancy, with about 200 c.c. of clotted old blood.

Case 3.—J. H., an 18-year-old nulligravida, was admitted to the service with the tentative diagnosis of ectopic pregnancy of three weeks' duration. She had fever, low abdominal pain, vaginal bleeding, anemia, and leucocytosis. The test for hematin was negative. The patient responded to medical management and was discharged with the diagnosis of acute salpingitis.

Case 4.—G. C., a 25-year-old multigravida, was admitted with the diagnosis of ruptured ectopic pregnancy. She was in shock and presented the findings of acute intra-abdominal hemorrhage. A positive test for hematin was obtained. Laparotomy revealed a ruptured right ectopic pregnancy with about 500 c.c. of blood in the peritoneal cavity.

Case 5.—M. E. Q., a 17-year-old nulligravida, had symptoms for three weeks prior to admission for a possible ectopic pregnancy. The test for hematin was negative. The patient responded to therapy for pelvic inflammatory disease and was discharged as improved with this diagnosis.

Case 6.—L. B., a 38-year-old multigravida, had symptoms of vaginal bleeding, pelvic pain, and fever for six weeks prior to admission for incomplete abortion or ectopic pregnancy. The test for hematin was negative. A few days later placental tissue was passed, and the diagnosis of incomplete abortion was confirmed.

CASE 7.—W. S., a 26-year-old multigravida, was admitted to the hospital with the diagnosis of ectopic pregnancy. She had vaginal bleeding, pain, a mass in the left adnexa, anemia, and leucocytosis. Hematin testing was negative. Dilatation and curettage of the uterus established the diagnosis of endometrial hyperplasia.

CASE 8.—M. S., a 20-year-old nulligravida, was admitted in shock for ruptured ectopic pregnancy. Her findings included bleeding, pelvic pain, delayed menses, marked anemia, and leucocytosis. The test for hematin was negative. The patient responded to supportive measures and was discharged with the diagnosis of acute pelvic inflammatory disease.

CASE 9.—J. J., a 36-year-old multigravida, was in shock when admitted with a diagnosis of ruptured ectopic pregnancy. She had vaginal bleeding, pelvic pain, anemia, and leucocytosis. Hematin testing and cul-de-sac aspiration were negative. She was discharged after treatment with the diagnosis of uncontrolled diabetes mellitus and severe acidosis.

CASE 10.—R. R., a 39-year-old multigravida, had findings suggestive of a ruptured ectopic pregnancy. She was in severe shock. Hematin testing was positive. The patient expired despite restorative measures prior to operation. The diagnosis was confirmed at autopsy.

CASE 11.—V. R., a 26-year-old nulligravida, had sudden pelvic pain and fainted six hours prior to admission with a diagnosis of suspected ruptured ectopic pregnancy. Hematin testing was positive. Laparotomy revealed about 300 c.c. of fresh and clotted blood in the peritoneal cavity, coming from a bleeding ruptured ovarian follicle.

CASE 12.—S. H., a 27-year-old white secundigravida, was admitted to the hospital with a tentative diagnosis of old ruptured ectopic pregnancy. The patient had amenorrhea for six weeks followed by marked right lower quadrant pain and vaginal spotting of blood for four days prior to admission. She also had slight fever, leucocytosis, and marked anemia. There was a 5 cm. soft to firm mass in the right cul-de-sac. Hematin testing was negaitve. Laparotomy revealed a retroperitoneal mass extending into the vagina. There was no ectopic pregnancy.

CASE 13.—L. L., a 31-year-old Negro multigravida, was admitted to the hospital with a history of amenorrhea for one month followed by vaginal bleeding of one day's duration the next two months. There was lower left quadrant cramping for three days prior to admission but no bleeding. There was no anemia or leucocytosis. Examination revealed a firm, irregular, movable mass extending to the umbilicus. There was a separate, soft, tender mass extending into the left cul-de-sac. A diagnosis of myomas of the uterus with pelvic abscess was made. Hematin testing was positive. A cul-de-sac aspiration following this revealed blood. Laparotomy revealed a ruptured left tubal pregnancy with myomas of the uterus.

CASE 14.—This 29-year-old Negro nullipara was admitted with a tentative diagnosis of retained secundines and pelvic abscess. The patient had amenorrhea for two months, followed by vaginal bleeding and pain for one month. Dilatation and curettage were done elsewhere for an incomplete abortion. Examination on admission now revealed the uterus to be soft and slightly enlarged. There was a 7 cm., tender, soft mass on the left, but no bulging in the cul-de-sac. The Hogben pregnancy test was positive. Hematin testing was positive. Laparotomy revealed an old ruptured ectopic pregnancy.

We must report four failures in our series. In one instance, hematin testing was negative when used as an aid in the differential diagnosis between ectopic pregnancy and an ovarian cyst. The patient went into shock shortly after the blood for testing was drawn. Laparotomy within a few hours revealed a recently ruptured ectopic pregnancy. We attribute the negative test to the assumption that the ectopic gestation had not ruptured at the time of testing.

In another instance, a patient with ruptured ectopic pregnancy was admitted to the surgical service. The only blood available for testing was that in the blood bank three days after it had been drawn.

The third case involved a patient with a ruptured spleen. Blood for hematin testing was obtained after the patient had received about 3,000 c.c. of intravenous fluids in efforts to combat shock. The test was negative. Laparotomy revealed the splenic rupture.

The fourth patient entered the hospital because of vaginal bleeding. Examination revealed bulging in the cul-de-sac, and on aspiration a slight amount of thin, brown fluid was obtained. Hematin testing was negative. At laparotomy a 5 cm., firm, encapsulated mass filled with 50 to 75 c.c. of clotted blood was found. No fetus or placenta was seen. Pathologic examination showed ghost villi in the tubal remnants, and a diagnosis of old ectopic gestation was made.

Comment

Up to this time the spectroscopic test for hematin in the peripheral blood has been carried out on 100 patients in whom the diagnosis was confusing. There were 73 Negro and 27 white patients in this series, and their ages varied from 15 to 62 years. A résumé of the conditions encountered in this series is shown in Table I.

TABLE I

Threatened abortion	18
Incomplete abortion	20
Pelvic inflammatory disease	10
Tubal pregnancy with intra-abdominal bleeding	10
Complete abortion	7
Pregnancy with acute pelvic inflammatory disease	4
Myoma with pelvic inflammatory disease	2
Low implantation of placenta	1
Septicemia with acute endometritis	2
Abdominal phlebitis	1
Ruptured tuboovarian abscess with peritonitis	3
Retroperitoneal mass	1
Threatened premature labor	1
Pelvic abscess	2
Pelvic inflammatory disease with peritonitis	4
Bleeding follicle of ovary	1
Pulmonary embolus	1
Tuboovarian abscess	4
Stab wound of stomach	1
Abdominal pregnancy	1
Hyperplastic endometrium with bleeding	1
Bleeding ulcer of stomach	1
Cerebral hemorrhage	1
Ruptured spleen	1
Ovarian cyst with infection	1
Pregnancy with pyelitis	1
Total	100

All of our patients with positive hematin tests have been operated upon. We have found no false positive tests, and all patients with positive tests had at least 100 c.c. of blood in the abdominal cavity. In all cases with negative hematin tests, with the exception of the four mentioned above, the subsequent course of the patient has suggested other diagnoses than those involving intraperitoneal hemorrhage.

The appearance of hematin in the blood stream is contingent upon several factors, and each of these may be sources of error. Clot formation is important in allowing enzymatic activity to break down the red blood cells with the liberation of hematin. Should this mechanism be faulty, there will be little or no hematin for absorption. Hemoglobin injected into the peritoneal cavity and absorbed as such will give negative hematin testing. The amount of blood loss is important also. We have been able to detect hematin in the blood of dogs within ninety minutes after injection of as little as 30 c.c. of heart blood into the peritoneal cavity. This small amount will give a positive test for about twenty-four hours. In severe hemorrhage, with the patient in shock, and for a variable period up to several days thereafter, several factors come into play and may alter the effects of testing. There is constriction of blood vessels with ischemia of the capillary bed.[5] The total blood flow may decrease to half the normal value.[6] There is a marked and rapid compensatory hydremia in an effort to support blood volume.[7-9] Activity of the patient is another factor influencing the findings.[10] These variables may alter absorption of hematin into the blood, in addition to causing sufficient dilution to make the test weak or negative.

We also make use of cul-de-sac aspiration and other means of diagnosis in suspected ectopic pregnancy with hemorrhage. Although intra-abdominal bleeding is usually reflected in the blood count by secondary anemia and leucocytosis, we have found that not too much reliance can be placed on the count. There have been several cases in which there was little or no anemia, and no leucocytosis. In addition, other types of bleeding and other conditions will produce similar blood pictures. Cul-de-sac aspiration is of decreasing value as a diagnostic procedure after the clot has become organized and free fluid is being absorbed.

Summary

An aid to the diagnosis of the extravasation of blood into a body cavity by means of the spectroscopic detection of hematin (reduced hemochromogen) in the peripheral blood is herein described. This is especially applicable to the diagnosis of ruptured ectopic pregnancy. A summary of the 100 patients upon whom we have carried out this test is reported. There were four failures, but there were no false positive reactions.

There are few laboratory tests that supplant clinical experience and judgment, and in this instance we are only exploring the possibility of an aid in diagnosis. At this time this report can only say that the theory and results coincide, and that we hope to perfect this technique further so that it may become a valuable laboratory procedure in the diagnosis of intra-abdominal accidents.

References

1. Cullen, T. S.: Contributions to Medical and Biologic Research (Osler Volume) **1**: 420, 1919.
2. Schumm, O.: Ztschr. f. phys. Chemie, Leipz. & Berl. **80**: 1, 1912.
3. Wendel, W. B.: J. Lab. & Clin. Med. **24**: 96, 1938.
4. Noyes, A. A.: Qualitative Chemical Analysis, ed. 9, New York, 1923, The Macmillan Company, p. 172.
5. Page, I. H., and Abell, R. G.: Am. J. Physiol. **143**: 182, 1945.
6. Richards, D. W., Jr.: N. Y. Acad. Med. **20**: 363, 1944.
7. Lawson, H., and Rehm, W. S.: Am. J. Physiol. **144**: 199, 1945.
8. Pride, M. P., Muntwyler, E., Griffin, G. E., Mantz, F. R., and Griffith, L.: Surgery **18**: 250, 1945.
9. Ebert, R. V., Stead, E. A., Gibson, J. G., II: Arch. Int. Med. **68**: 578, 1941.
10. Elman, R., and Davey, H. W.: Proc. Soc. Exper. Biol. & Med. **56**: 14, 1944.

THE DURATION OF LABOR: MEAN, MEDIAN, AND MODE

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THE figures cited in textbooks, and ordinarily taught, for the duration of labor are eighteen hours in primigravidas and twelve hours in multiparas (Stander, DeLee-Greenhill, Beck). These are mean or average values, calculated simply by adding up the total hours occupied by all labors in a large series and dividing by the number of labors. Although mean or average figures are often valuable, it is well known to statisticians that they may sometimes be very misleading in that, under certain circumstances, they may not yield typical and truly representative values. Let us consider, as an extreme example, a community of 300 families, made up of a hamlet of 290 families, surrounded by 10 country estates each occupied by a millionaire. If the incomes of the families in the hamlet ranged from $1200 to $2600, as shown in Table I, and those of the wealthy group were $50,000 each, the mean or average income would be $3230—obviously a figure which is not at all representative of a typical family in the community. While this is an exaggerated and artificial example, it helps to recall that extreme values, which lie far outside the usual run, may so distort the mean or average of a series of observations as to render it quite meaningless.

TABLE I. CRUDE EXAMPLE SHOWING HOW A FEW EXTREME VALUES IN ANY SERIES TEND TO DISTORT AVERAGE OR MEAN FIGURES

NUMBER OF FAMILIES	INCOME OF EACH FAMILY	TOTAL INCOME
50	$1,200	$60,000
100	1,500	150,000
80	1,600	128,000
20	1,800	36,000
10	2,100	21,000
20	2,400	48,000
10	2,600	26,000
10	50,000	500,000
300		$969,000

Average income—$3230; Median income—$1550; Modal income—$1500

When, in any series of variate magnitudes, a few of the values lie far outside the range of most of the values, the median and mode of the series may be more representative and informative figures than the mean or average. The median for any series of observations, it will be recalled, is the center value above and below which fall exactly half the individual values. It is particularly useful as a measure of central tendency in a series in which it is desired to suppress the influence of extreme or unusual values. By the mode of any series is

meant the value which shows the greatest frequency of occurrence, it being assumed that seriation provides a reasonably smooth frequency distribution. In the above example, the median may be taken as $1550, while the mode is obviously $1500. Clearly, either of these figures is much more representative of the income of the typical family in the community mentioned than is the mean of $3230.

It is the purpose of this paper to report figures on the mean, medial, and modal duration of labor in 15,533 consecutive cases of parturition which occurred at the Johns Hopkins Hospital between Jan. 1, 1937 and Dec. 31, 1945. In this series, there were 758 cases in which either the duration of labor was unknown, or cesarean section was performed. These were discarded, leaving 14,775 cases which were grouped according to race and parity as follows:

	White	*Negro*	*Total*
Primiparas	4243	3278	7,521
Multiparas	4227	3027	7,254
	8470	6305	14,775

The criterion used for the onset of labor was regular, painful uterine contractions observed by the patient. This entails, of course, a certain source of error, but in the main such errors would tend to counterbalance each other. In the present analysis only the total duration of labor will be considered.

The calculated mean or average durations of labor for the above groups are as follows:

	White	*Negro*
Primiparas	13.04 hours	15.15 hours
Multiparas	8.15 hours	10.27 hours

Fig. 1 shows the frequency distribution curve of 4243 labors in white primiparas together with the perpendiculars indicating the mean, median, and modal durations of labor for this group. It will be seen that the curve is not the symmetrical type of normal frequency distribution, but is skewed to the right by reason of a small number of extremely long labors; in other words, by a few values which lie far outside the range of most of the values. Actually the limit of this curve would be 118 hours—the longest white primiparous labor in this series. The median duration of labor for this group was found to be 10.59 hours —almost 2½ hours less than the mean. The mode was 7 hours, slightly more than half the mean.

Fig. 2 shows the rates at which labor progressed in the four groups. It will be noted that about 65 per cent of white primiparas had labors of less than 13.04 hours (mean or average for this group) and that about the same percentage of multiparas had been delivered after less than their respective averages. These curves define the median durations of labor for the four groups as follows:

	White	*Negro*
Primiparas	10.59 hours	12.37 hours
Multiparas	6.21 hours	7.31 hours

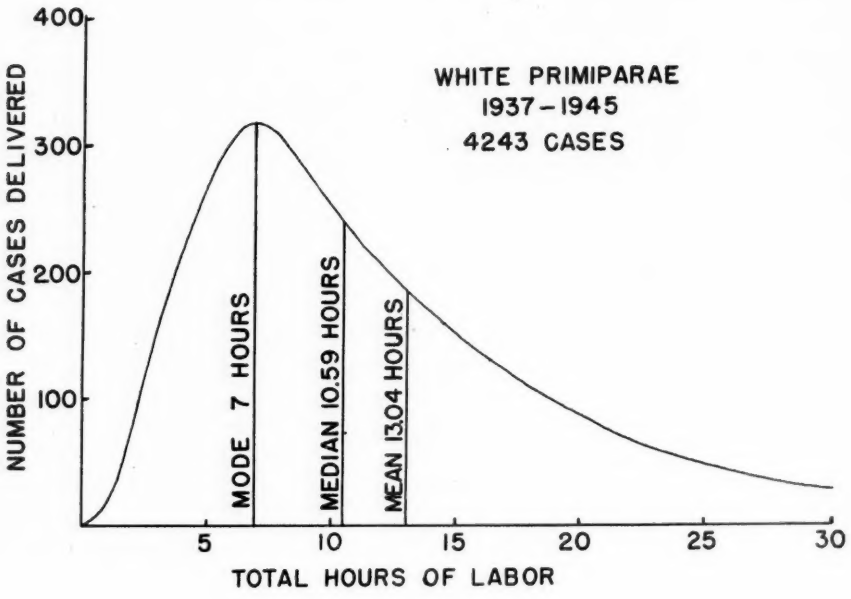
400
300
200
100
NUMBER OF CASES DELIVERED
WHITE PRIMIPARAE
1937–1945
4243 CASES
MODE 7 HOURS
MEDIAN 10.59 HOURS
MEAN 13.04 HOURS
5
10
15
20
25
30
TOTAL HOURS OF LABOR

Fig. 1.

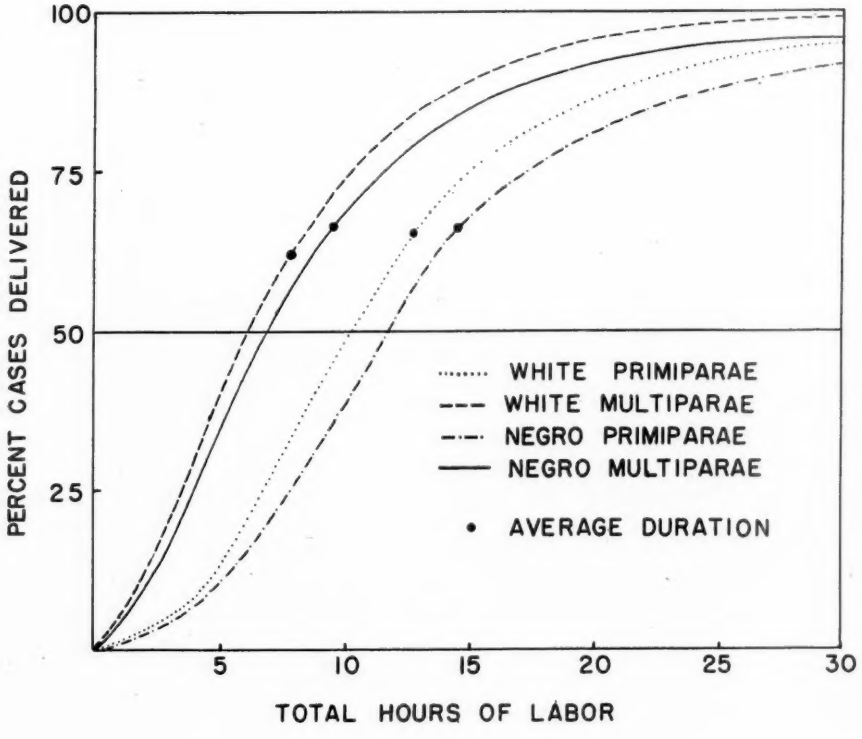
100
75
50
25
PERCENT CASES DELIVERED
WHITE PRIMIPARAE
WHITE MULTIPARAE
NEGRO PRIMIPARAE
NEGRO MULTIPARAE
AVERAGE DURATION
5
10
15
20
25
30
TOTAL HOURS OF LABOR

Fig. 2.

The frequency distribution curves for the four groups are shown in Fig. 3. The data on which these curves are based are given in Table II. The peaks of these curves define the modal durations of labor as follows:

	White	*Negro*
Primiparas	7 hours	7 hours
Multiparas	4 hours	4.5 hours

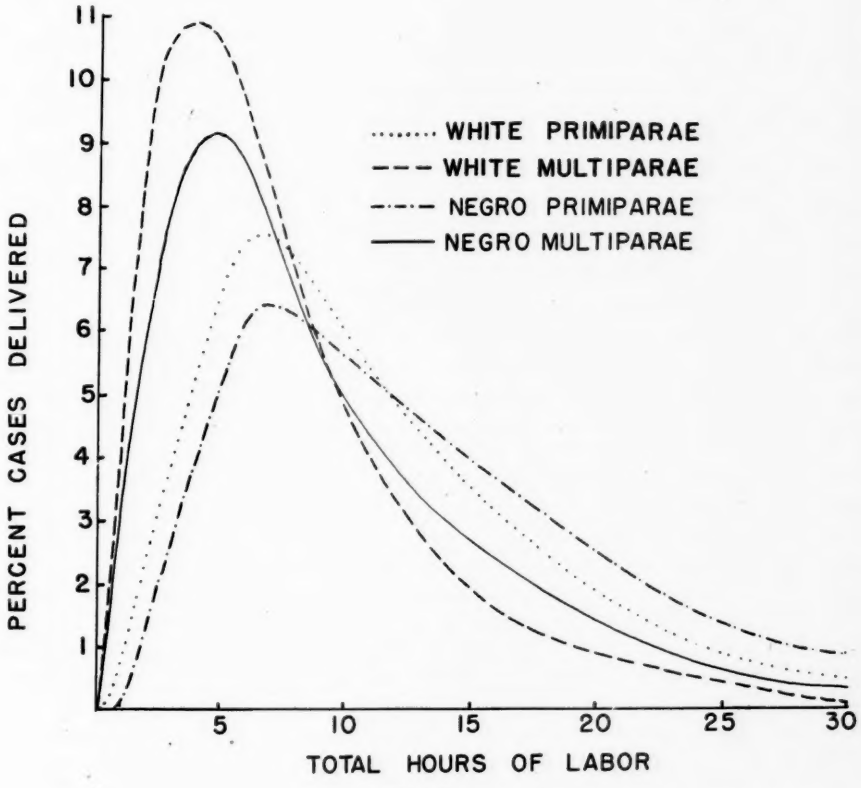

Fig. 3.

TABLE II. FREQUENCY DISTRIBUTION OF 14,775 CASES ACCORDING TO DURATION OF LABOR, RACE, AND PARITY

HOURS OF LABOR	WHITE PRIMIPARAS	WHITE MULTIPARAS	NEGRO PRIMIPARAS	NEGRO MULTIPARAS
0- 3	216	949	150	545
4- 6	735	1274	447	793
7- 9	903	824	559	560
10-12	700	493	505	318
13-15	504	236	418	227
16-18	391	169	338	199
19-21	242	96	236	111
22-24	165	64	169	83
25-27	112	47	107	57
28-30	67	20	84	29
31 and over*	208	55	265	105

*The longest labor for white primiparas was 118 hours, for white multiparas 87 hours, negro primiparas 136 hours and negro multiparas 131 hours.

It should be noted that the peaks for the Negro women do not represent as high a per cent of the total group as those for the white, but the curves are more skewed to the right. This explains the significant difference both in the mean and median durations of labor between white and negro, although the modes are essentially the same—this difference being attributable to the greater number of abnormal and prolonged labors in negresses.

With the mean, median, and modal durations of labor thus established for this series, the question arises as to which of these indices is the most descriptive and useful. If complete appreciation of a variate series is to be had, it is necessary, in the opinion of statisticians, to know the characteristics of the entire distribution, but if reliance is placed on one centering constant alone, and the material is definitely skew, the median is usually the most informative value. Applied to the duration of labor, these statements, together with the findings in the present study, indicate the desirability of laying more stress on the median duration of labor than has been done in the past. Certainly, if 65 per cent of labors terminate in less than the average time, the latter index taken alone is misleading. The main desiderata here would seem to be chiefly those figures which are most descriptive of the *typical* duration of labor in primigravidas and in multiparas, and there can be no question that the medians give a much truer picture in this regard than do the means or averages.

It is interesting, nevertheless, to compare the average values calculated in this series with the accepted values of 18 hours in primigravidas and 12 hours in multiparas, and more particularly with the averages found by Peckham in a series of 13,658 consecutive deliveries from Jan. 1, 1907 to Dec. 13, 1929 in the Johns Hopkins Hospital (Table III). These figures would tend to indicate that modern improvements in obstetrical technique and prenatal care have reduced significantly the average duration of labor. To explain fully this difference from the statistical data at hand would be impossible, but certain factors immediately come to mind which probably tend toward shortening the average duration of labor. Before 1935, the incidence of forceps deliveries in this clinic was less than 13 per cent. Recently, the popular use of elective low forceps for the delivery of primigravidas has raised this figure to 38 per cent. In the past decade, the cautious use of pituitrin stimulation in cases of uterine inertia has eliminated many very long labors from this series. These labors of exceedingly long duration would unduly increase the average duration as pointed out above. In the past few years, there has been much stress laid on the importance of diet in prenatal care. High protein diets, supplemented with vitamins and minerals, and low in salt content, may shorten the average duration of labor. These observations tend to explain to a certain degree the decrease noted in the average duration of labor as shown in Table III.

TABLE III. COMPARISON OF THE MEAN DURATION OF LABOR CALCULATED AT THE JOHNS HOPKINS HOSPITAL

	WHITE PRIMIPARAS	WHITE MULTIPARAS	NEGRO PRIMIPARAS	NEGRO MULTIPARAS
Jan. 1, 1907 to Dec. 13, 1929 (Peckham)	16.57 hours	10.91 hours	17.66 hours	12.49 hours
Jan. 1, 1937 to Dec. 31, 1945	13.04 hours	8.15 hours	15.15 hours	10.27 hours

Conclusions

1. Previous calculations of the average duration of labor are misleading because of the incidence of prolonged labors, which distorts the frequency distribution of the cases delivered and of hours labor.

2. The median and modal durations of labor are presented as being more statistically significant than the mean or average, and certainly more in keeping with the experience of obstetricians.

3. In white primiparas, the mean was found to be 13.04 hours, the median 10.59 hours, and the mode 7 hours; in white multiparas, the mean was 8.15 hours, the median 6.21 hours, and mode 4 hours. In negro primiparas, the mean was calculated as 15.15 hours, the median 12.37 hours, and the mode 7 hours; while in negro multiparas, the corresponding findings were 10.27, 7.31, and 4.5 hours.

4. The average duration of labor is longer in negro than in white patients because of the greater incidence of prolonged labors in the former.

5. Recent improvements in obstetrical technique and prenatal care have significantly shortened the average duration of labor.

The author wishes to thank Dr. Margaret Merrell for her many helpful suggestions in the preparation of this paper.

References

Beck, A. C.: Obstetrical Practice, ed. 3, Baltimore, 1942, the Williams and Wilkins Company.
DeLee, J. B., Greenhill, J. P.: The Principles and Practice of Obstetrics, ed. 8, Philadelphia, 1943, W. B. Saunders Company.
Foederl, V.: Monats. f. Geburts. u. Gynäk. **102**: 65-79, 1936.
Kerr, A., Jr.: Am. J. Obst. & Gynec. **45**: 950-960, 1943.
Peckham, C. H.: Am. J. Obst. & Gynec. **24**: 744-750, 1932.
Pomerance, W., and Daichman, E.: Am. J. Obst. & Gynec. **40**: 463-466, 1940.
Schuitema, D. M.: Am. J. Obst. & Gynec. **46**: 707-711, 1943.
Stander, H. J.: Textbook of Obstetrics. Stander's 3rd revision, New York, 1945, D. Appleton-Century Co., Inc.
Wadlow, E. E.: Am. J. Obst. & Gynec. **39**: 749-756, 1940.

STUDY OF THE INCIDENCE AND OCCURRENCE OF SYMPTOMS OF VAGINAL TRICHOMONADS AND VARIOUS SPECIES OF YEAST IN PREGNANCY*

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A STUDY evaluating the efficacy of treatment of *Trichomonas vaginalis* vaginitis with tyrothricin suppositories[1] yielded considerable data concerning the incidence of, and symptoms caused by, vaginal trichomonads and various species of yeast. Since relatively few surveys have been published on certain aspects of the subject, it was thought that an analysis of the data might add to the general information.

The incidence of *Trichomonas vaginalis* has been reported by many workers; the average seems to be about 25 per cent.[2] Symptoms of pruritus and discharge are not always associated with the trichomonads. In fact, they may be absent in 47 to 87 per cent of patients with vaginal trichomoniasis.[3]

Yeastlike fungi were isolated from the vaginas of 32 per cent of pregnant patients and 14 per cent of gynecologic patients by Carter and Jones[4] in 1937. Again, in 1940, Carter et al.[5] found 33 per cent of obstetric patients had yeasts in their vaginal tracts. Carter et al.[5] were the first to study the relationship of symptoms to genera and species of fungi. They found that in those patients who carried Saccharomyces or Cryptococci there were no symptoms referable to a mycotic infection and that only patients who carried one of three Candida species, albicans, stellatoidea, and tropicalis, had symptoms.

The purpose of this paper is to present the incidence of *Trichomonas vaginalis* and species of yeastlike fungi found in this survey and to study any association of symptoms with the two types of infection.

Materials and Methods

The patients examined were those who presented themselves to the Charity Hospital Obstetric Clinic for the first visit of their prenatal care. All were in a low economic stratum, Negro patients constituting the vast majority of those seen. Parity and the stage of pregnancy were varied.

Patients were questioned as to the occurrence of pruritus, burning on urination, and vaginal discharge. Frequently, because of reticence or indifference, no discharge was reported by the patient, but was seen on examination. No study was made for causes of symptoms other than trichomonads and yeasts.

Material from the walls of the vagina, posterior fornix, and the mouth of the cervix was collected on a sterile swab which was rubbed over the surface of a tube of Sabouraud's glucose agar before being deposited into a tube with

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Thanks to Marion S. Felknor, B.S., for technical assistance.

one ml. sterile saline. The saline swab was examined by wet mount immediately, or within ten minutes, for *Trichomonas vaginalis*. The Sabouraud's agar was incubated at room temperature for two or three days and examined for yeast colonies. The method of Martin et al.[6] was followed for the identification of Candida species; Cryptococci and true yeasts were not identified as to species.

Findings

Incidence of Trichomonas Vaginalis and Yeastlike Organisms.—As has been reported by Johnson et al.,[1] of 1197 pregnant women who were examined for vaginal trichomonads, 321, or 26.8 per cent, were found to harbor these organisms. A higher incidence was found in Negro women than in white (Table I).

TABLE I. INCIDENCE OF TRICHOMONAS VAGINALIS IN PREGNANCY

	WHITE	NEGRO	TOTAL
Total examined	255	942	1,197
Positive	40	281	321
% positive	15.7	29.8	26.8

Over a period of six months, March through September, 244, or 37 per cent, of 667 pregnant women were found infected with yeast or yeastlike organisms (Table II). There were 13.2 per cent more Negro women than white who carried yeast. No difference was found in the incidences during the spring and the summer months.

TABLE II. INCIDENCE OF YEAST INFECTION IN PREGNANT WOMEN OVER A PERIOD OF SIX MONTHS

	MAR. 22–JUNE 30	JULY 1–SEPT. 30	TOTAL
No. White Females			
Examined	97	72	169
Positive	26	20	46
% positive	26.7	27.7	27.2
No. Negro Females			
Examined	261	237	498
Positive	104	94	198
% positive	40.0	39.6	40.4
Total			
Examined	358	309	667
Positive	130	114	244
% positive			37.0

Table III presents the incidence of double infection found in 654 persons. As is to be expected from the above findings, the Negro group had the higher percentage of such infections.

TABLE III. INCIDENCE OF CONCURRENT YEAST AND TRICHOMONAS INFECTION IN PREGNANT FEMALES OVER A PERIOD OF SIX MONTHS

	NUMBER EXAMINED	NUMBER POSITIVE	% POSITIVE
White	169	5	2.9
Negro	485	59	12.1
Total	654	64	9.8

The number of the various species of Candida and the number of true and false yeasts found in this survey are shown in Table IV. Unlike the incidence

reported in North Carolina by Carter et al.[5] and by Jones and Martin,[7] who found the greatest number of women were infected by *C. stellatoidea* and the next highest number by *C. albicans*, the species found most often in New Orleans was *C. albicans*, and then *C. stellatoidea*. Moreover, there were fewer of the other species of Candida and yeasts found in this survey than in the study in North Carolina. It was also noted that a large number of these species were not quite typical in their cultural characteristics. This will be considered later.

TABLE IV. NUMBER OF VARIOUS SPECIES OF YEASTS FOUND IN 667 PREGNANT WOMEN

GENUS AND SPECIES	NO. TYPICAL	NO. ATYPICAL	TOTAL
Candida albicans	68	34	102
Candida stellatoidea	65	26	91
Candida tropicalis	7	1	8
Candida Krusei	0	1	1
Candida parakrusei	1	0	1
Candida sp. (unidentified)	3	0	3
Total Candida	144	62	206
Cryptococci sp.	37		37
True yeast	1		1
Total yeast strains			244

Incidence of Symptoms.—The association of symptoms of pruritus, burning, and discharge with vaginal trichomonads and yeasts was studied in 360 cases. Since individuals suffering from other causes of these symptoms were not excluded from the survey, the 167 women having neither of the infections in question were considered a reference group. There were 84, or 50 per cent, of these who had symptoms (Table V). Of 60 persons with trichomonads, 45, or 75 per cent, had symptoms. This finding seems significant when compared with the reference group. Of 98 persons with yeast infections, 60, or 61 per cent, had symptoms. However, this number is too close to the reference point to have any significance. It is interesting to note that 213 of the total 360 persons reported symptoms, and that of the 147 individuals having no apparent disease, 63 harbored at least one of the two types of organisms being studied.

TABLE V. INCIDENCE OF SYMPTOMS IN PERSONS EXAMINED FOR TRICHOMONADS AND YEAST

	NO. HAVING TRICH.	NO. HAVING YEAST	NO. HAVING BOTH TRICH. AND YEAST	NO. HAVING NEITHER TRICH. NOR YEAST	TOTAL
No. with symptoms	45	60	25	83	213
No. without symptoms	15	38	10	84	147
Total	60	98	35	167	360

It was thought that a study of the various species in relation to the symptoms might yield some information which was obscured by considering the yeasts as a whole. Table VI presents the number of persons, with and without symptoms, who were infected with each species. Of 48 individuals harboring *C. albicans*, 31, or 64.4 per cent, reported symptoms. Of 27 with *C. stellatoidea*, 16, or 59.2 per cent, had symptoms. It is obvious that neither of these has a significant difference in the incidence of symptoms.

TABLE VI. INCIDENCE OF SYMPTOMS IN PERSONS INFECTED WITH YEAST ONLY

SPECIES	NO. WITH SYMPTOMS	NO. WITHOUT SYMPTOMS	TOTAL
C. albicans	31	17	48
C. stellatoidea	16	11	27
C. tropicalis	4	1	5
C. Krusei	0	1	1
Candida sp. (unidentified)	0	1	1
Cryptococci	9	7	16
Total	60	38	98

As mentioned above, there were a number of species which were atypical (Table IV). The group harboring only yeast was analyzed to ascertain whether these atypical organisms occurred only in asymptomatic persons. It may be seen in Table VII that the ratio of atypical to typical strains is approximately the same in persons with pruritus and discharge as in persons without symptoms.

TABLE VII. COMPARISON OF APPEARANCE OF SYMPTOMS IN PERSONS INFECTED WITH TYPICAL AND ATYPICAL CANDIDA SPECIES

SPECIES	WITH SYMPTOMS		WITHOUT SYMPTOMS		TOTAL
	TYPICAL	ATYPICAL	TYPICAL	ATYPICAL	
C. albicans	20	11	11	6	48
C. stellatoidea	10	6	6	5	27
C. tropicalis	3	1	1	0	5
C. Krusei	0	0	0	1	1
Total	33	18	18	12	81

Using the same group of persons, the magnitude of yeastlike infection was also compared with the occurrence of symptoms. This quantitative estimation was based on the number of colonies found on the surface of the Sabouraud's slant, 50 colonies being considered the dividing line between a transitory or carrier state and true infection. Table VIII shows that of those who have less than 50 colonies, there is no difference in the number of persons with and without symptoms. However in the group having more than 50 colonies on their cultures, there are almost twice as many persons who have symptoms as those who do not. In particular is this true of the group carrying *C. albicans.* It may be concluded that the quantitative degree of infection of at least one species of Candida is associated with the incidence of symptoms.

TABLE VIII. COMPARISON OF APPEARANCE OF SYMPTOMS IN PERSONS WITH LIGHT AND HEAVY YEAST INFECTIONS

SPECIES	NO. OF PERSONS WITH LESS THAN 50 COLONIES		NO. OF PERSONS WITH MORE THAN 50 COLONIES		TOTAL
	WITH SYMPTOMS	WITHOUT SYMPTOMS	WITH SYMPTOMS	WITHOUT SYMPTOMS	
C. albicans	9	6	22	11	48
C. stellatoidea	5	4	11	7	27
C. tropicalis	0	1	4	0	5
C. Krusei	0	0	0	1	1
C. sp.	0	0	0	1	1
Cryptococci	3	3	6	4	16
Total	17	14	43	24	98

In the method used for identifying Candida species, only one colony is picked from the Sabouraud's slant. This means that if two species are present, one is missed. In a small series of persons who came to the clinic regularly for

other treatment, cultures were taken over a period of one to eight weeks. In two of 20 persons thus examined, two species were recovered at different times. In five persons, unidentified species which closely resembled the persistent, typical culture of each, were found. Thus, there is a definite chance that two or more Candida species can be carried simultaneously, and that the second is missed when only one colony is picked for identification.

Comment

The incidence of *Trichomonas vaginalis* found in this survey is much the same as that found in other parts of the country. The higher incidence in Negro persons than in white does not indicate racial predilection but only emphasizes that spread of infection is aided by crowded living conditions and the general lack of personal cleanliness prevalent in the underprivileged.

The incidence of vaginal mycosis was approximately the same as that found by Carter et al.[4, 5] and by Martin et al.[6] in Durham, North Carolina, ours being only slightly higher.

It was noted during the war that all types of fungi abound in the tropical countries. There was no opportunity in this survey to compare vaginal mycotic incidence with temperature or humidity, since the weather conditions in New Orleans were approximately the same in the spring and summer months. The average temperature for the spring was 75.9 degrees F. and that for summer 81.6 degrees F., with a maximum difference of 10 degrees between the averages of the six months. Likewise there was a maximum difference of only 11 per cent between the average relative humidity of each of the six months. The average humidity of New Orleans and that of Durham are also only slightly different. Thus theories of a correlation between the incidence of vaginal mycoses and humidity and temperature cannot be proved by these data. However, there is at least a negative value here, in that the findings are in accord with such theories.

No explanation can be offered for the different relative incidence of *C. albicans* and *C. stellatoidea* in the two cities. It is more than probable that these differences are quite within the realm of chance.

In studying association of symptoms with the two diseases, it was necessary to compare the infected groups with the uninfected group. The reason for this was that due to the large size of the clinic, no routine examination was made for other infections causing the same symptoms. It was found that 50 per cent of women uninfected with vaginal trichomonads or yeasts have symptoms of pruritus or discharge. Therefore it was expected that 50 per cent of the infected persons might also have symptoms which were not caused by their specific infection. An increase of 25 per cent in the incidence of symptoms therefore seems significant and implies that the trichomonads are associated with symptoms. It has been proved by Trussel and Plass[8] that *Trichomonas vaginalis* can cause such symptoms. However, an increase of only ten per cent, as in the case of yeast infection, cannot indicate an association of the infection with symptoms.

In the same manner, an analysis was made of the data concerning symptoms in persons with the various species of Candida (Table V). However, increases over the base line of 14.4 and 9.2 per cent, for *C. albicans* and *C. stellatoidea,* respectively, cannot be interpreted as being significant. There were too few persons in the group having *C. tropicalis* to make any comments other than to point out that all but one person had symptoms. The group harboring Cryptococci had almost the same number having symptoms as those that did not. It may be seen that these data take the direction of agreement with the work of Carter[5]; that is, *C. albicans, C. stellatoidea,* and *C. tropicalis* are associated with symptoms while the other yeasts are not.

There was a possibility that strains of Candida which were atypical might be considered rough, and like the rough Pneumococci, be avirulent. However, no such correlation could be made (Table VI). According to these data, atypical cultural characteristics of the Candida species do not imply change in virulence.

There was definite correlation of magnitude of infection with symptoms. It is possible that a carrier state may exist for a time and then change to a state of disease with symptoms. This change would probably be dependent upon changes in the condition of the host. Or it is possible that the patients with fewer numbers of organisms were examined at the beginning of the infection and that symptoms would appear when the number of organisms increased. It would be of interest to take numerous cultures of a few such persons over a period of time to study these two theories.

Since there is a possibility that the patient can carry two different species of yeasts, such a project as suggested above would be very desirable. It would eliminate some of the errors occurring in surveys made from single examination and single colony identification.

Summary and Conclusions

1. *Trichomonas vaginalis* was found in 321, or 26.8 per cent, of 1197 pregnant women who were examined by the wet mount method.

2. Cultures of yeast or yeastlike organisms were obtained from the vaginas of 244, or 37 per cent, of 667 pregnant women.

3. Both trichomonads and yeast were found in 64, or 9.8 per cent, of 654 pregnant women.

4. More Negro women than white harbored the two infections. This fact was undoubtedly not due to racial predilection but to differences in mode of living and personal hygiene.

5. *Candida albicans* and *C. stellatoidea* comprised the majority of strains of yeasts found in this survey, *C. albicans* being the greatest in number.

6. Although symptoms of discharge, burning, and pruritus can be caused by both *T. vaginalis* and certain species of yeasts, their mere presence does not indicate coincidence of symptoms.

7. No definite relationship of symptoms with any species of yeast was found. However, the data pointed in the direction of agreement with Carter, that *C. albicans, C. stellatoidea,* and *C. tropicalis* are associated with symptoms while the Cryptococci are not associated with pruritus and discharge.

8. No relationship of atypical strains of Candida with the asymptomatic state was found.

9. The quantitative degree of infection with yeasts, particularly *C. albicans,* was discovered to be connected with the appearance of symptoms of pruritus and discharge.

10. The method of collecting yeast samples, using only one examination of the patient and picking only one colony for identification, is reliable within limits as a basis for studying incidence. Definite conclusions may be drawn from such a survey when the numbers are large; however, the chance of missing a concurrent infection with another species of yeast might cause erroneous deductions when the numbers are small.

11. A study should be made to determine whether those persons having no symptoms and harboring a few organisms are in a carrier state or in one of incipient infection.

References

1. Johnson, C. G., Douglas, J. W., and Mayne, Ruth: Treatment of *Trichomonas Vaginalis* with Tyrothricin. In Press.
2. Trussell, Ray E., and Johnson, Garth: Puerto Rico J. Pub. Health and Trop. Med. **20:** 289-305, 1944-45.
3. Cornell, E. L., Goodman, L. J., and Matthies, M. M.: Am. J. Obst. & Gynec. **22:** 360, 1931.
4. Carter, Bayard, and Jones, C. P.: South. M. J. **30:** 294, 1937.
5. Carter, Bayard, Jones, Claudius P., Ross, R. A., and Thomas, Walter L.: Am. J. Obst. & Gynec. **39:** 213-226, 1940.
6. Martin, Donald S., Jones, Claudius P., Yao, K. F., and Lee, L. E., Jr.: J. Bact. **34:** 99-128, 1937.
7. Jones, Claudius P., and Martin, Donald S.: Am. J. Obst. & Gynec. **35:** 98, 1938.
8. Trussell, R. E., and Plass, E. D.: Am. J. Obst. & Gynec. **40:** 883-890, 1940.

A STUDY OF THE USE OF PENICILLIN IN PREMATURE RUPTURE OF THE MEMBRANES

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IT HAS been shown that penicillin reaches the human amniotic fluid and fetal tissues when administered to the mother. As a result, it has been suggested that it might be employed as a protection against intrauterine infection following premature rupture of the amniotic membranes.[1-4]

The present investigation was undertaken in order to determine specifically the effect of penicillin upon (1) the bacterial content of the cervix at delivery, (2) the latent period between the rupture of the membranes and the onset of labor, (3) maternal morbidity, and (4) fetal mortality.

Methods and Material

The study was made from approximately one thousand consecutive admissions to the Obstetric Service of the Hospital of the University of Pennsylvania. Those qualifying were patients whose membranes had ruptured at home, and whose uterine contractions had not started prior to admission to the hospital. In each case, rupture of the "bag of waters" was confirmed by a positive "dye" (bromthymol blue) test.[5] There were no cases of prolapse of the cord. All patients fell into labor spontaneously; none were examined vaginally. All women were confined to bed on admission to the hospital; alternate ones received 12,500 units of penicillin* intramuscularly every three hours from the time of admission until delivery. Oral temperatures were recorded every four hours day and night.

Fifty-seven patients were studied; 29 received penicillin and 28 received none. In no case was it necessary to abandon the study in the interest of the patient. One woman in each group stopped leaking fluid, did not go into labor, and was discharged from the hospital.

At delivery, cervical cultures were taken from 24 of the 29 patients receiving penicillin and from 21 of the 28 women who received none.

Table I shows the frequency with which various bacteria were observed in the 57 patients. Pathogens were present in the cervices of both treated and control patients; gonococci were present in one of the untreated patients. Only two (6.9 per cent) of the patients receiving penicillin became morbid,† whereas six (21.4 per cent) of the control group did so.

*The penicillin sodium was furnished through the courtesy of the Department of Medical Research, Winthrop Chemical Company.

†Any patient with a temperature rise to 100.4 degrees F. on any two days, exclusive of the first 24 hours post partum, was considered morbid.

TABLE I. BACTERIA PRESENT IN THE CERVICES OF ALL PATIENTS AT THE TIME OF DELIVERY

ORGANISMS	PATIENTS 29 TREATED	28 CONTROL
Staphylococcus albus	6	13
Staphylococcus aureus	1	1
Staphylococcus hemolyticus	2	2
Micrococcus flavus	1	1
Diphtheroid bacillus	11	5
Bacillus lactis aerogenes	3	–
Bacillus proteus	3	–
Bacillus coli communis	18	4
Yeast cells and bacilli	1	–
Streptococcus pyogenes hemolyticus	1	1
Streptococcus viridans unidentified	1	3
Streptococcus nonhemolyticus	7	11
Streptococcus morphology (unidentified)	1	1
Hemophilus	5	5
Goncoccus	–	1
No growth	2	2

The morbid patients (Table II) showed a variety of bacteria. Penicillin-sensitive and penicillin-resistant organisms were cultured from the cervices of both the treated and untreated women.

TABLE II. BACTERIA PRESENT IN THE CERVICES OF MORBID PATIENTS AT THE TIME OF DELIVERY

ORGANISMS	MORBID PATIENTS 2 TREATED	6 CONTROLS
Staphylococcus albus	2	3
Staphylococcus aureus	1	1
Diphtheroid bacillus	2	3
Bacillus coli communis	2	3
Yeast cells and bacilli	1	–
Streptococcus pyogenes hemolyticus	–	1
Streptococcus viridans unidentified	1	–
Streptococcus nonhemolyticus	1	4
Hemophilus	2	3
Gonococcus	–	1
Total different organisms cultured from cervix	12	19

The number of hours between the rupture of the membranes and the onset of labor is shown in Table III.

The thirty-sixth week of gestation is taken as a dividing line between the term and premature gestations.

In general, the latent periods were not affected by penicillin in either the term or premature gestations. This suggests that penicillin has little if any oxytocic effect on the uterus at or near term. The average latent period was approximately 23 per cent longer in the case of the pregnancies which terminated prematurely than in the case of the patients who went to term.

The effect of the latent period on morbidity is indicated in Table IV. There was no definite relationship between the length of the latent period and the frequency of maternal morbidity. It will be noted, however, that all morbidities occurred in patients whose latent periods exceeded twenty hours.

TABLE III. TIME INTERVAL BETWEEN RUPTURE OF THE MEMBRANES AND ONSET OF LABOR

INTERVAL (HOURS)	GESTATION OF PATIENTS			
	NO. TREATED		NO. CONTROLS	
	UNDER 36 WEEKS	OVER 36 WEEKS	UNDER 36 WEEKS	OVER 36 WEEKS
1-10	-	3	-	1
11-20	2	4	-	4
21-30	1	4	1	4
31-40	2	2	1	3
41-50	1	2	1	1
51-60	-	2	1	-
61-70	-	-	-	3
71-80	-	-	-	-
81-90	1	-	-	1
91-100	1	2	2	1
131-140	-	-	-	2
191-200	1*	-	-	-
240	-	-	1*	-
Total patients	9	19	7	20
Average latent period (hours)	43.7	33.4	58.3	43.0

*Omitted in average.

TABLE IV. MORBIDITY IN RELATION TO DURATION OF INTERVAL BETWEEN RUPTURE OF MEMBRANES AND DELIVERY

INTERVAL (HOURS)	PATIENTS			
	NO. TREATED		NO. CONTROLS	
	MORBID	NONMORBID	MORBID	NONMORBID
1-10	-	3	-	1
11-20	-	6	-	4
21-30	1	4	3	2
31-40	-	4	1	3
41-50	1	2	-	2
51-60	-	2	1	-
61-70	-	-	-	3
71-80	-	-	-	-
81-90	-	1	-	1
91-100	-	3	-	3
101-110	-	-	-	-
131-140	-	-	1	1
191-200	-	1*	-	-
231-240	-	-	-	1*
Total patients	2	26	6	21
Average latent period (hours)	35	36.6	50	50.5

*Not included in the average.

There were three infant deaths (Table V). Two of the fetuses died in utero. The mother (A.C.) of one of these received penicillin. This fetus was found to have a negative culture from its heart blood. Postmortem examination showed congenital heart disease and evidence of possible erythroblastosis fetalis. The mother (D. F.) of the second infant who died in utero received no penicillin. A blood culture from this infant's heart was positive for hemolytic staphylococcus albus. The cause of its death was believed to be due to septicemia.

The third infant died of pneumonia, which disease was confirmed at postmortem. Difficulty of delivery and a prolonged apnea were considered contributory causes of this death. The mother had received penicillin.

TABLE V. INFANT DEATHS

PATIENT	PENICILLIN	GESTATION WEEKS	LATENT PERIOD HOURS	MORBID	INFANT				
					DEATH	WT. GRAMS	CAUSE	CULTURE HEART BL.	POST MORTEM
A. C. No. 23224	Yes	32	196	No	Intrauterine	1670	Congenital heart disease—erythroblastosis	No growth	Congenital heart disease, erythroblastosis
D. F. No. 23368½	No	34	36	No	Intrauterine	2190	Septicemia	Hem. staph. albus	Negative (cause undetermined)
R. S. No. 24777	Yes	40	52	No	Neonatal	3640	Prolonged labor, high midforceps, apnea	Not taken	Pneumonia

Summary

A study of the use of penicillin in premature rupture of the membranes is presented. The effects of penicillin on the bacteriology of the cervix, the latent period between the rupture of the membranes and the onset of labor, maternal morbidity, and fetal mortality are shown.

Conclusions

Penicillin administered to patients with premature rupture of the membranes has little, if any, effect upon the bacteria cultured from the cervix at or near term.

It has little, if any, oxytocic effect on the term or near-term uterus.

Premature rupture of the membranes of less than twenty hours' duration was not followed by maternal morbidity. Beyond that length of time there is no definite relationship between duration of premature ruptured membranes and maternal morbidity.

Administration of penicillin to patients with premature rupture of the membranes influences favorably the frequency of maternal morbidity. Therefore its routine use under such circumstances is indicated.

References

1. Herrell, W. E., Nichols, D. R., and Heilman, D. H.: J. A. M. A. **125**: 1003, 1944.
2. Green, H. J., and Hobby, G. L.: Proc. Soc. Exper. Biol. & Med. **57**: 282, 1944.
3. Hutter, A. M., and Parks, J.: AM. J. OBST. & GYNEC. **49**: 663, 1945.
4. Woltz, J. H. E., and Zintel, H. A.: AM. J. OBST. & GYNEC. **50**: 338, 1945.
5. King, A. G.: AM. J. OBST. & GYNEC. **30**: 860, 1945.

SPLENECTOMY IN PREGNANCY: ITS HEMATOLOGIC INDICATIONS AND OBSTETRIC MANAGEMENT

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THE necessity for splenectomy during pregnancy in the therapy of certain hematologic dyscrasias is relatively rare, and surgery under such circumstances is still a questioned procedure. The present discussion of the problem is based on three splenectomies performed on pregnant women for critical hematologic indications. While this is a small group, we know of no similar consecutive series. During the past seventeen years special emphasis has been placed upon the role of the spleen in human disease in the Hematology Clinic at this University. From a large clinical experience in a wide variety of hematologic dyscrasias, some 210 therapeutic splenectomies have been recommended and accomplished.[1, 2] The three pregnant women in this series who presented aggravated hypersplenic syndromes are here considered from the obstetric point of view.

Splenectomy for blood dyscrasias complicating pregnancy has been reported ten times. In four of these cases the indication was Banti's syndrome, and in six thrombocytopenic purpura. An additional, unreported case operated upon for congenital hemolytic icterus has come to our attention,[3] and undoubtedly other cases exist which have not been recorded.

Hesseltine in 1930[4] and McKenzie in 1936[5] each reported a splenectomy performed for Banti's disease during pregnancy. The outcome in each case was successful. In 1937, Serbin[6] reported two patients operated upon following this diagnosis. Finn in 1944[7] collected from the literature four cases of splenectomy for thrombocytopenic purpura in pregnancy. These had been reported by Berstein, Newman and Hitzig (1939), Phythyon and Lartz (1943), Polowe (1944) and Gromen's reference to a splenectomy in pregnancy for thrombocytopenic purpura performed by Garlock (date not given). In 1946, Nordland, Ylvisaker, Larson, and Reiff[8] added a case, as did Dinsmore and Dutlinger.[9]

Case Reports

CASE 1.—V. M., a 21-year-old white woman was admitted to the hospital with a chief complaint of bruises and purpuric spots on the legs and abdomen, and fatiguability. She was a gravida i, seven months pregnant at the time, and had been under the care of her physician since the third month. There had been no vaginal bleeding, but vitamin K had been administered without benefit for the purpuric areas on the legs and for irregular bleeding of the gums which the patient had suffered.

Physical examinaiton revealed evidences of recent bleeding of the gums, multiple purpuric spots over the legs and abdomen, and numerous petechiae of the mucous membranes. The fundus of the uterus was just above the umbilicus and the fetal heart sounds were of good quality. Pelvic measurements were normal and the remainder of the physical examination was not remarkable.

Preoperatively the patient's platelet count ranged between 6,000 and 12,000 (normal for the method used, 750,000+ per c.mm.). White cell count, differential, red count, and hemoglobin were all normal for the duration of gestation. Bone marrow studies showed abundant young and mature megakaryocytes, a normal quantitative differential with a shift to the left of both red and white elements consistent with the patient's pregnancy. Prothrombin and vitamin C deficits were ruled out. The diagnosis of essential thrombocytopenic purpura was made and the patient was prepared for splenectomy. Whole blood transfusions of 500 c.c. were given the day before and the day of surgery; 10 mg. of Proluton were administered daily from the day before operation throughout the patient's hospital stay.

Operation was carried out under cyclopropane and ether anesthesia. The spleen was relatively posterior and had a moderately short pedicle. The spleen was removed and extensive exploration carried out for accessory spleens. None were located, the wound was closed, and the patient returned to her bed in good condition. The postoperative course was complicated only by a small wound hematoma which did not become infected and which was drained on the tenth day. The platelet count improved slowly but steadily following the splenectomy. Postoperatively on the day of operation, the platelets rose to a high of 39,600; during the next three days to 48,020, 61,600 and 70,560 respectively. By the fifth postoperative day the platelet count had risen to 306,000 and the following day it was 497,700 per c.mm. Throughout the remainder of the patient's stay in the hospital the circulating thrombocytes ranged between 400,000 and 800,000 per c.mm. with complete cessation of all clinical manifestations of purpura.

At the conclusion of the operation the fetal heart rate was 160. Two hours later it had returned to 130, and remained normal throughout the hospital course. There were no painful uterine contractions and no vaginal bleeding. The Proluton was discontinued upon discharge from the hospital, and the remainder of the patient's antepartum course was uneventful. Two months postoperatively she went into labor spontaneously and delivered a normal term viable fetus with no difficulty, and without excessive blood loss. No blood counts are available on the infant, but it was without purpuric symptoms and has manifested no hemorrhagic tendencies. The subsequent, nonobstetric course of this patient has been reported elsewhere.[10]

Case 2.—M. J. H., aged 23 years, a primigravida four months pregnant, was admitted with the chief complaints of intermittent jaundice, extreme exhaustion, and exertional dyspnea. The family history revealed that the patient's father had had congenital hemolytic icterus, and probably her paternal grandfather also. Two brothers had histories of intermittent attacks of jaundice. The patient's own previous attacks had been chiefly related to exhaustion and fatigue, but during this pregnancy there had been an associated definite icterus. During a routine antepartum checkup, her physician discovered that the hemoglobin and red count were falling abnormally and referred her to the hospital at once for further studies.

Examination on admittance revealed no icterus, marked pallor of the skin and mucous membranes, no petechiae. The spleen was palpable below the costal margin and tender. The uterine enlargement was proportionate to the patient's pregnancy. The red count was 2,250,000, hemoglobin 9.5 Gm., white count was

11,000 with a normal distribution. The reticulocyte level ranged between 16 and 23 per cent. Red cell fragility started at 0.550 and was complete at 0.267 (normal for this method 0.412 to 0.300). Urinalysis was negative; icteric index 15; van den Bergh was direct negative, indirect, 1.62. A diagnosis of congenital hemolytic icterus, subacute activity, was made and the patient prepared for splenectomy.

Proluton, 10 mg. a day, was started and continued until the patient was discharged from the hospital. Cyclopropane anesthesia was employed and the spleen removed without difficulty. Exploration failed to reveal accessory spleens, and no abnormality of the gallbladder, bile ducts, or liver was noted. Postoperatively the patient received 1,000 c.c. of washed cells. Erythrocyte destruction ceased immediately, and the red cells rose slowly to 3,200,000 per c.mm. Convalescence was uneventful. The patient was discharged on her twelfth postoperative day, there having been no evidence of abnormal uterine activity in the meantime. The patient continued on to term, went into labor spontaneously, and delivered with outlet forceps after fourteen hours. The baby had a normal neonatal course without evidence of icterus. Blood count on the third day of life revealed 14,300 leucocytes with a normal differential; an erythrocyte count of 4,930,000 per c.mm., with a reticulocyte level of 5.6 per cent. The hemoglobin was 20.4 Gm. and the platelet level 1,397,120. The baby was discharged with the mother on the tenth day, having regained birth weight. At the age of 6 months a hematologic checkup was obtained on the baby which revealed no pathology. The reticulocyte level at that time was 0.8 per cent and the red cell fragility was within normal limits.

CASE 3.—H. B., a 31-year-old primigravida entered the hospital when five months pregnant with the complaints of purpuric spots over legs and abdomen and of epistaxis. The duration of her hemorrhagic manifestations and of her pregnancy were identical, the first bleeding from the nose having followed her last menstrual period. The patient also had had moderately severe nausea and vomiting the first four months, which were beginning to subside at the time of hospital admittance.

Physical examination revealed a well-developed and well-nourished white woman with multiple petechiae over skin and mucous membranes. The uterus was 22 cm. above the symphysis, fetal motion and heart sound identifiable. Pelvic measurements were normal.

There was no familial history of purpura, and, although the patient had worked as a welder until two months prior to the onset of her bleeding tendencies, the history suggested the pregnancy as the most probable precipitating mechanism. This was supported by the bone marrow findings, which failed to reveal any evidence of toxic damage to the normal elements. The platelet count ranged between 21,000 and 47,000, the marrow revealed megakaryocytosis, the remainder of the blood picture being compatible with the pregnancy. The basal metabolic rate was minus 11 and the prothrombin level 115 per cent. The hematologic diagnosis was essential splenic thrombocytopenic purpura, and the patient was prepared for splenectomy.

A program of thyroid and Proluton was started preoperatively, and 500 c.c. of fresh blood were given prior to surgery. Under cyclopropane anesthesia the spleen was exposed, found to be moderately enlarged, and removed without difficulty. An accessory spleen was found at the hilus. Gentle exploration revealed no other intra-abdominal abnormalities and the wound was closed with only moderate oozing.

The surgical and obstetric convalescence was uneventful. There were no uterine cramps, and no vaginal bleeding. The patient was allowed out of bed

on the third postoperative day and was discharged the twelfth day. The platelet response was satisfactory. By the evening of the day of surgery the count had risen to 60,000 and the following morning it was 311,300. It remained over 300,000 for the next five days and between 100,000 and 200,000 for the duration of the patient's hospitalization.

The patient continued under direct antepartum observation. Her course was uneventful, and her platelet count ranged between 200,000 and 350,000 at each visit. She was admitted at term in active labor and had a short (seven hour), relatively easy primiparous labor concluded with outlet forceps and left mediolateral episiotomy. Blood loss was small, and the postpartum course uneventful. The episiotomy healed by primary intent. Blood counts on both the mother and baby at the time of delivery and later showed no abnormality. The baby was weaned and was discharged with a gain over birth weight.

Discussion

It cannot be stressed too frequently that the pregnant patient demonstrating hemorrhagic tendencies should have the benefit of a complete hematologic investigation. The symptomatic administration of vitamin K to the first of these three patients without proper study succeeded only in delaying specific treatment. Complete evaluation of the peripheral blood, sternal marrow aspiration with supravital studies, the adrenalin test for splenic contraction, and the biopsy this provides of the cells sequestered by the spleen all contribute essential data. In the hemorrhagic states hypoprothrombinemia and hypovitaminosis C must be ruled out, as well as allergic or amyelophthisic thrombocytopenias.

In the gravid patient who has had such studies and whose diagnosis is firmly established, however, we do not feel that the presence of the pregnancy alters the hematologic indications for splenectomy. The two diagnoses represented by the cases here reported—congenital hemolytic icterus and thrombocytopenic purpura hemorrhagica—are the most frequently met indications. Primary splenic neutropenia and panhematopenia[11] may also be met in the pregnant patient.

Wolff and Limarzi[12] have recently stated that in thrombocytopenic purpura "splenectomy is best done following the pregnancy and during a remission of the disease, but may be performed if the patient is seen during the first trimester." They feel that this represents "a conservative attitude toward the pregnancy." With this dictum, as well as its reasoning, the present writers disagree. In our opinion, the hemorrhagic state represents a greater hazard than does the operation of splenectomy irrespective of the trimester of the pregnancy, and true conservatism indicates a correction of the hematologic disorder as soon as the diagnosis is established and the patient properly prepared.

While purpuric states may not influence postpartum blood loss,[7, 13] antepartum and intrapartum hemorrhage remains a constant threat, and intrauterine fetal death from retroplacental hemorrhage has been reported.[6] On the other hand, splenectomy, even with thorough search for accessory spleens, should not precipitate labor. While each of these patients was on an "antiabortion regime" of corpus luteum products, thyroid, and adequate sedation, it remains our conviction that gentleness of intra-abdominal manipulation at the time of surgery

constitutes the most important single measure to prevent the onset of uterine contractions.

The relationship between the pregnancy and the hematologic status is of interest. Where the two conditions are closely related by history (Case 3) the pregnancy may be considered the precipitating factor.[14] It is not, however, the causative factor, the cause remaining splenic sequestration and destruction. Insofar as the baby is concerned, the hereditary nature of the hemolytic icterus is well known. With respect to thrombocytopenic purpura, we feel, as previously expressed by Wiseman, Doan and Wilson,[15] that the condition may be congenital, but that it has not yet been established as hereditary.

Summary

Three cases of splenectomy performed during pregnancy are presented. Two of these were for thrombocytopenic purpura and one for congenital hemolytic icterus. In each case the pregnancy proceeded to term and a normal child was delivered. The place of splenectomy in the treatment of hematologic disorders occurring during pregnancy is discussed.

The authors wish to express their appreciation to Dr. B. K. Wiseman for permission to report on two of his private patients. Dr. G. M. Curtis performed the splenectomies and Dr. Charles Pavey delivered one of the patients.

References

1. Doan, C. A., and Wright, C. S.: Blood **1**: 10, 1946.
2. Doan, C. A.: Edwin R. Kretschmer Memorial Lecture, Proc. Inst. Med. Chicago **16**: 178, 1946.
3. Trenis, J. W., Kunath, C. A., and Wilcox, E. A.: Personal communication.
4. Hesseltine, H. C.: Am. J. Obst. & Gynec. **20**: 77, 1930.
5. McKenzie, C. H.: Am. J. Obst. & Gynec. **32**: 486, 1936.
6. Serbin, W. B.: Am. J. Obst. & Gynec. **34**: 486, 1937.
7. Finn, W. T.: Am. J. Obst. & Gynec. **48**: 497, 1944.
8. Nordland, M., Ylvisaker, R. S., Larson, P., and Reiff, R.: Minnesota Med. **29**: 166, 1946.
9. Dinsmore, R. S., and Dutlinger, R. P.: Cleveland Clin. Quart. **13**: 128, 1946.
10. Curtis, G. M., and Movitz, D.: Ann. Surg. **123**: 276, 1946.
11. Wiseman, B. K., and Doan, C. A.: Ann. Int. Med. **16**: 1097, 1942.
12. Wolff, J. R., and Limarzi, L. R.: Am. J. Obst. & Gynec. **51**: 447, 1946.
13. Barnes, A. C.: Am. J. Med. Sc. **213**: 463, 1947.
14. Doan, C. A.: West Virginia M. J. **41**: 121, 1945.
15. Wiseman, B. K., Doan, C. A., and Wilson, S. J.: J. A. M. A. **115**: 8, 1940.

ARRHENOBLASTOMA OF THE OVARY*

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NINETY-FOUR cases of arrhenoblastoma of the ovary have been reported in the literature. No single theory of the pathogenesis of these tumors has been universally accepted. The two theories most widely supported at this time are those advanced by Meyer,[1] who suggested that arrhenoblastomas arise from latent male elements in the ovary, and the teratomatous theory first suggested by Popoff.[2] The report of another case seems justified because of the debatable pathogenesis of these tumors, and because of the interesting problems which arise in conjunction with the multiplicity of tissues found on pathologic examination. Endocrine interrelationships and the mode of action of these hormone-producing tumors are also debatable.

Dr. D. D. Odell of Bryan, Ohio, has very kindly furnished the entire tumor for study, and has supplied the following history, physical examination, and follow-up. Dr. Edwin F. Hirsch and Dr. John I. Brewer have given invaluable aid in the study of these tissues.

The patient, Mrs. V. C., aged 23 years, white, married, gravida i, entered the Cameron Hospital, Bryan, Ohio, on the service of Dr. D. D. Odell. Two years prior to hospital admission, the patient had a normal spontaneous delivery of a full-term pregnancy. Following delivery there was a resumption of her normal menstrual cycle, and then her periods became more frequent, occurring at two-week intervals, and finally progressing to almost continuous spotting. One year prior to admission she became completely amenorrheic, and at the same time first noticed that her voice was becoming appreciably deeper. Six months before operation a marked growth of hair developed on the patient's upper lip and about her breasts. There was a noticeable enlargement of the lower abdomen, and the patient believed herself to be pregnant.

Physical examination revealed a well-developed and well-nourished white woman, 23 years of age. She did not appear to be acutely ill. Her voice was a rich baritone, and there was a definite growth of hair on the upper lip and chest. Pelvic examination revealed a freely movable, somewhat cystic, smooth, round mass that extended to the umbilicus. The mass seemed to be more prominent on the left side. The uterus was of normal size and was palpated separately from the mass. A preoperative diagnosis of arrhenoblastoma of the ovary was made.

On Sept. 26, 1945, under general anesthesia, an abdominal section was performed by Dr. D. D. Odell. There was a multiloculated cystic and solid left ovarian tumor. The right ovary and tube were normal. Exploration of both suprarenal regions and of the abdomen revealed no tumor or metastases. A left salpingo-oophorectomy was done.

*Presented before the Chicago Gynecological Society, March 21, 1947.

Pathologic Examination.—The tumor had solid and multiloculated cystic tissues and weighed 14 pounds. It was blue-gray and the intact capsule was smooth. On many surfaces made by cutting there were multiple smooth cysts ranging from a few millimeters to six centimeters in diameter. In the lumens of some of the cysts was a mucoid substance. The cystic structures were separated by fibrous septums. About 40 per cent of the tumor was solid, and these portions were well demarcated, firm, and tan-brown in color. There were numerous large regions of hemorrhage and necrosis.

Microscopic examination was made of multiple sections cut from sixty-five blocks taken from representative regions of the tumor. The tissues were fixed in formalin and stained with hematoxylin-eosin. Mayer's mucicarmine, Laidlaw's silver stain, phosphotungstic acid and Foote's modification of Masson's trichrome stain. Sections were also stained after the method of Bennett[3] with phenylhydrazine to demonstrate 17-ketosteroids. Fat stains were made of frozen sections from many regions. A scant ovarian stroma along the periphery was normal, but there were no primordial or developing follicles. In one section a structure was observed which may have been an atretic follicle, but this was not positively identified. There were many corpora albicantia. The solid portions were tumor tissues with a wide range in morphologic structures. The tumor cells, in a background of edematous reticular stroma, were generally of two types. In regions in which the stroma predominated there were spindle-shaped cells with scant cytoplasm and oval vesicular nuclei. In some places these cells were arranged in parallel rows forming retelike structures. (Fig. 1.) The second predominant type of tumor cell was polygonal, medium in size, with oval or round coarsely granular nuclei and a moderate amount of neutrophilic cytoplasm. Mitotic figures were rare. The polygonal cells were in groups, or islands, and arranged in sheets, cords, strands, or whorls in most regions, but in others they appeared as mosaics lying in tissue crevices and with bizarre lumenlike structures. Throughout the tumor were foci of edema, and in these the appearance of the cells was considerably altered. The lobules of edematous cellular tissue were subdivided by fibrous connective tissue septums which surrounded small groups of tumor cells. The tumor cells themselves had signs of degeneration, with pyknotic nuclei, vacuolated cytoplasm, and in some instances disintegration of the cell membrane. (Fig. 2.) These regions of edema appear similar to published photomicrographs of adrenal-like ovarian tumors. There were also transition stages from the tumor cells which showed no degeneration to the vacuolated degenerating cells lying in the foci of edema described above. In the transition zones, single cells or small aggregates with pyknotic nuclei and vacuolated cytoplasm were seen in the midst of a large number of normal tumor cells. Retrogressive changes seemed to be most marked in the large cells. Multinucleated forms were seen in some regions.

Wherever loose connective tissue was found there were cells which resembled the interstitial cells of the testes. (Fig. 3.) These cells occurred singly and in groups. Their nuclei were round, though occasionally irregular, and the nuclear membrane was prominent. The nucleolus was usually eccentric. In Sudan-stained sections the interstitial cells and the polygonal tumor cells were laden with lipid droplets. The cystic structures described grossly were lined by low cuboidal or keratinized epithelium.

In some sections were small foci of gland structures lined by tall columnar epithelium. (Fig. 4.) These nonciliated epithelial cells had oval nuclei arranged regularly at the base of the cells. They contained no silver-reducing granules. Interspersed throughout the columnar epithelium of the glands were goblet cells. In the lumina of the glands was a homogenous mucoid substance. The goblet cells and the substance in the lumen of the glands stained darkly with Mayer's mucicarmine stain.

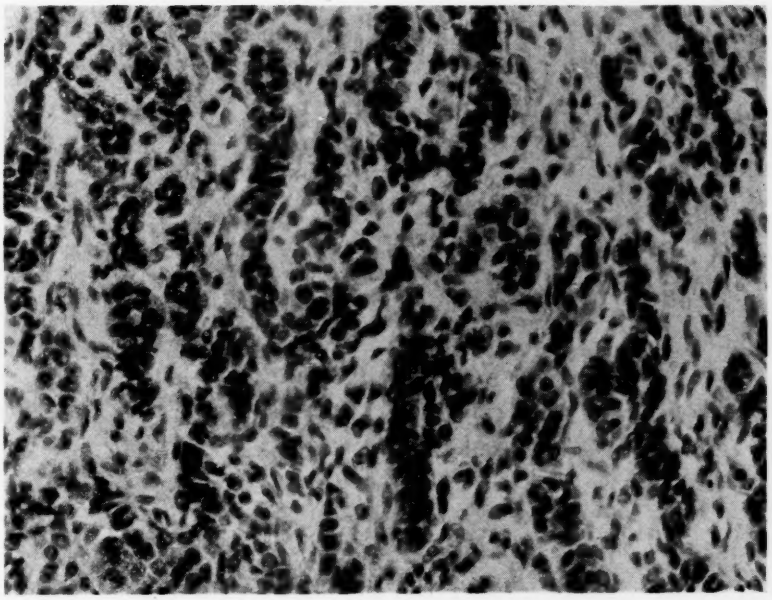

Fig. 1.—Tumor cells forming retelike structures are present in many sections.

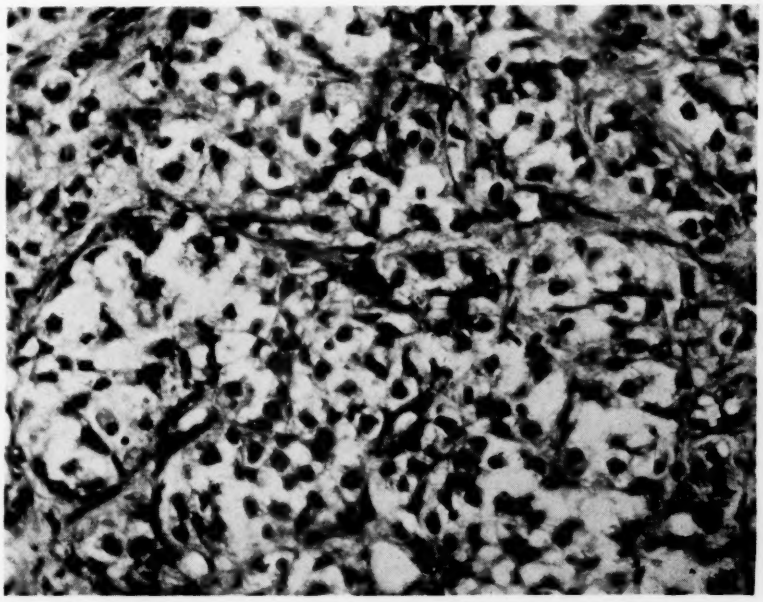

Fig. 2.—Some of the tumor cells in regions of edema have vacuolated cytoplasm, pyknotic nuclei, and dissolution of the cell membrane, indicative of degeneration.

The tumor had a reticular stroma, varying from coarse to fine fibers in character, and was widely infiltrated with plasma cells and lymphocytes. There were many small blood vessels whose lumina were filled with red blood cells.

The sections stained with phenylhydrazine had a marked yellow color, as did adrenal tissues stained by similar solutions at the same time. Neutral tissues (heart, spleen, thyroid) stained simultaneously as controls did not become yellow.

Examination of the patient eighteen months after removal of the tumor showed an almost complete regression of the hirsutism. Menstruation began four months after excision of the tumor, and her menstrual cycles have remained normal. Pelvic examination revealed no abnormalities. Her general health is excellent.

In classifying arrhenoblastomas, most authors follow the grouping proposed by Meyer,[1] who divided these tumors into three types, a well-differentiated, an undifferentiated, and an intermediate or transitional group. Norris[4] believed that it is impossible so to classify arrhenoblastomas because of the wide morphologic variations in individual specimens. Because of the widely variable histologic pattern of this tumor, it does not fit into any one of Meyer's groups.

There has been some discussion in the literature of the criteria for the diagnosis of arrhenoblastoma, and recent authors have been of the opinion that in the light of present knowledge both clinical and pathologic confirmation is required. The diagnosis in the case presented here is substantiated by the histologic examination of the tumor and by the clinical evidence of masculinization followed by resumption of feminine characteristics and regression of masculinization after excision of the tumor.

The sections stained with phenylhydrazine resulted in positive findings. This does not indicate the specific presence of corticosterones, but does suggest that in the tumor tissues are substances which are chemically consistent with the corticosterones or with similar substances which have been isolated from the adrenal glands but which have no cortical activity. Clinical laboratory methods for the determination of 17-ketosteroids in patients with arrhenoblastomas have yielded widely varying and inconclusive results. Several investigators, among them Frazer and Forbes,[5] Talbot and Butler,[6] and Mallory,[7] report normal values. Recently Jones and Everett[8] found increased values. It has been suggested by some authors that the virilizing factor in arrhenoblastoma is some steroid, not yet isolated, which is not a 17-ketosteroid. Kanter and Klowans[9] found a markedly decreasd blood and urinary sodium, which contrasts with the definite increase in blood sodium values reported by Cutler, Power, and Wilder[10] in patients with the adrenogenital syndrome. Other laboratory procedures have proved to be of little value.

The multiplicity of tissue elements demonstrated in the histologic examination of this tumor suggest a possible teratomatous origin. Krock and Wolferman[11] in a review of seventy cases in the literature report that in twenty-four, or 34 per cent, tridermal tissue elements were found. When it is considered that the majority of arrhenoblastomas are large, and that most histologic studies are based on a very small portion of the tumor, the percentage of reports of teratomatous elements might be appreciably higher if the entire tumor were studied histologically. The work of many other authors, including Curtis,[12] Hartz,[13] and McLester,[14] has supported the teratomatous theory.

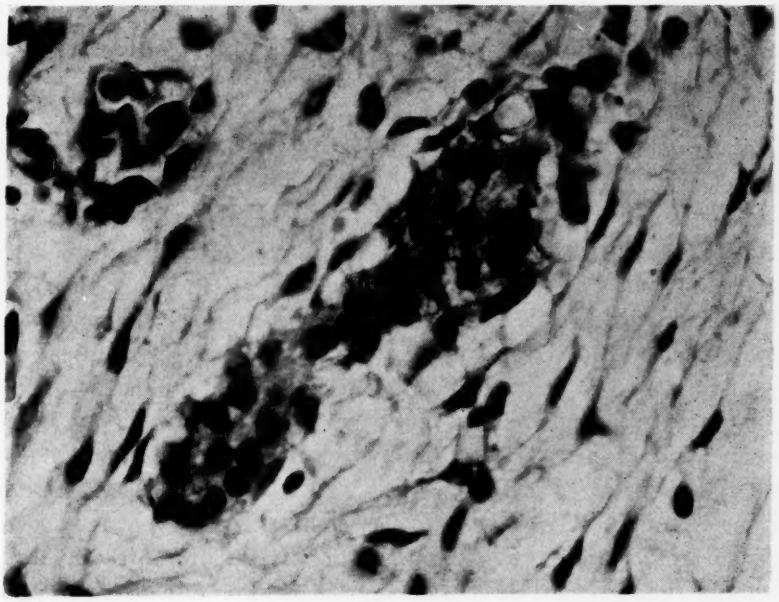

Fig. 3.—Interstitial cells, resembling the Leydig cells of the testes, are found throughout the tumor wherever there is loose connective tissue.

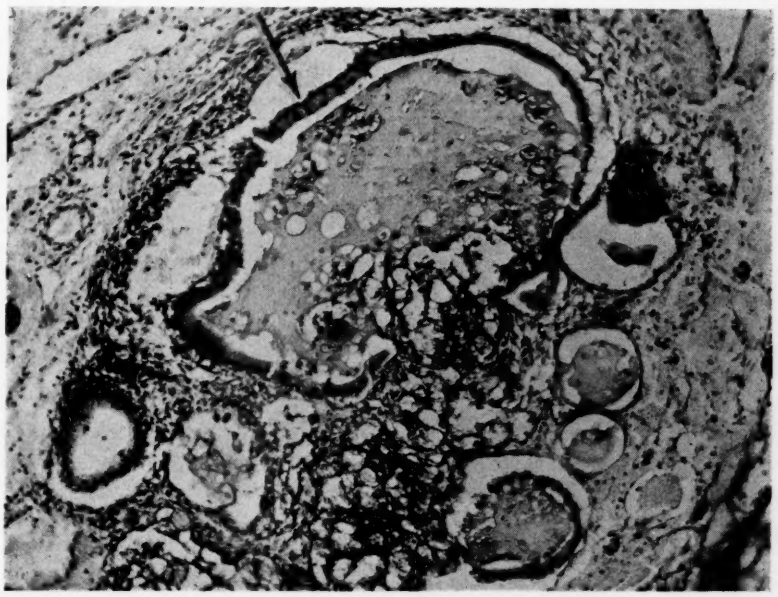

Fig. 4.—Gland structures lined by tall columnar epithelium and goblet cells (arrow) are seen in some regions. In the lumina of the glands is a mucoid substance.

The manner in which arrhenoblastoma and other hormone-producing ovarian tumors produce changes in the secondary sex characters of their hosts is not known. That the solution to this problem lies in endocrine interrelationships is emphasized by the experimental work on intersexuality done by Greene,[15] Crew,[16] and Lille.[17] Other clinical and experimental reports indicate the involvement of the pituitary gland, although the significance of this fact is not clear. Huffman[18] concluded that the androgenic effect of the male sex hormone given by injection produces changes in the female genitals which are secondary to pituitary changes, and that these effects last for only a short time after adrogenic stimulation is discontinued. Huffman[19] also substantiates the work of Hamilton and Wolfe[20] on basophilic changes in the pituitary gland after injections of testosterone proprionate. There is also clinical evidence of pituitary involvement. Similar basophilic pituitary changes were found at autopsy in the case of arrhenoblastoma reported by Norris.[4] Canelo and Lisser[21] report a case of arrhenoblastoma which presented clinically many of the metabolic changes associated with Cushing's syndrome. These same metabolic changes, according to Kepler and his associates,[22] are an integral part of the clinical picture of the masculinizing adrenal-like tumors of the ovary. Whether or not this close association of masculinizing ovarian tumors with the pituitary gland is significant, or whether it is merely incidental to the production of a virilizing hormone by the tumor, is not known.

Summary

1. A case of arrhenoblastoma of the ovary is presented with the diagnosis based on a combination of clinical and pathologic features.

2. The multiplicity of tissue elements found on histologic examination of the tumor suggest the possibility of a teratomatous origin.

References

1. Meyer, R.: Am. J. Obst. & Gynec. **22**: 697, 1931.
2. Popoff, N. U.: Arch. Path. **9**: 31, 1930.
3. Bennett, H. S.: Am. J. Anat. **67**: 151, 1940.
4. Norris, E. H.: Am. J. Cancer **32**: 1, 1938.
5. Fraser, R. W., Forbes, A. P., Albright, F., Sulkowitch, H., and Reifenstein, E. C.: J. Clin. Endocrinol. **1**: 234, 1941.
6. Talbot, N. B., and Butler, A. M.: J. Clin. Endocrinol. **2**: 724, 1942.
7. Mallory, T. B.: New England J. Med. **221**: 349, 1939.
8. Jones, G. S., and Everett, H. S.: Am. J. Obst. & Gynec. **52**: 614, 1946.
9. Kanter, A. E., and Klowans, A. H.: Am. J. Cancer **40**: 474, 1940.
10. Cutler, H. H., Power, M. H., and Wilder, R. M.: J. A. M. A. **111**: 117, 1938.
11. Krock, F., and Wolferman, S. J.: Ann. Surg. **114**: 78, 1941.
12. Curtis, A. H.: Am. J. Obst. & Gynec. **52**: 129, 1946.
13. Hartz, P. H.: Am. J. Path. **21**: 1167, 1945.
14. McLester, J. B., Arch. Int. Med. **57**: 773, 1936.
15. Greene, R. R.: J. Clin. Endocrinol. **4**: 335, 1944.
16. Crew, F. A. E.: Proc. Roy. Soc. London s.B. **95**: 256, 1923.
17. Lille, F. R.: Science **43**: 611, 1916.
18. Huffman, J. W.: Endocrinology **29**: 77, 1941.
19. Huffman, J. W.: Am. J. Obst. & Gynec. **40**: 675, 1940.
20. Wolfe, J. M., and Hamilton, J. B.: Endocrinology **21**: 603, 1937.
21. Canelo, C. K., and Lisser, H.: Endocrinology **24**: 838, 1939.
22. Kepler, E. J., Dockerty, M. B., and Priestly, J. T.: Am. J. Obst. & Gynec. **47**: 43, 1944.

STERILIZATION FAILURE WITH EXTERNAL MIGRATION OF THE OVUM*

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METHODS of tubal sterilization have varied widely from occlusion of the uterine ostium to various techniques of ligation (with and without crushing), tubal section, excision, and closure or burial of the fimbriated extremity. Few of them have stood the test of time without some failure. For a number of years we practiced the Walthard (Madlener) method until some failures were encountered. Then, after witnessing the technique used by Norman Miller of Ann Arbor, that of double tubal ligation of short loops without crushing, we tried that over a period of the past five years. We found the method entirely successful until we encountered this case which we suspected was a failure until proved otherwise at operation, as reported below. We have had, however, one other case of failure with this technique.

Polak reported a case of intrauterine pregnancy in 1910 which occurred after double salpingectomy. He took occasion to remark about "the vagaries of the fecundated ovum in selecting a location for its development, and the persistency and penetrability of the spermatozoon in its effort to reach the object of its search." Although not the first to be reported, his case serves to emphasize the fact that there have been pregnancies occurring after almost every type of tubal sterilization. Pregnancy has been reported even after supracervical hysterectomy.

The following case of sterilization failure is of interest because pregnancy occurred after double tubal ligation on the one side, eleven years after salpingo-oophorectomy had been performed on the other.

Case Report

Mrs. A. N., aged 40, gravida iii, was first seen by us in 1938. Her menstrual history was normal, regular every 28 days, 2½ days' duration, scant in amount. Appendectomy and right salpingo-oophorectomy were performed in 1933. In 1936, she had delivered premature twins (seven months) which did not survive, and in 1937 a full-term stillborn breech. A third degree tear occurred during the extraction of the breech resulting in a rectovaginal fistula. Both of these confinements were cared for elsewhere, before we had been consulted. She first came under our care for her third pregnancy which was terminated on March 17, 1939, by elective low cervical cesarean. This was her first living child.

She again became pregnant in 1943 and a second elective low cervical cesarean was performed on May 17, 1944. At operation, the right uterine horn

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from which the adnexa had been removed in 1933, was covered with dense adhesions. A loop of the small intestine was found adherent, forming a sharp kink. The adhesions were freed and the bowel liberated. Sterilization was performed by catgut ligation of two small loops of the left tube, without crushing, according to the method described above. (Fig. 1.)

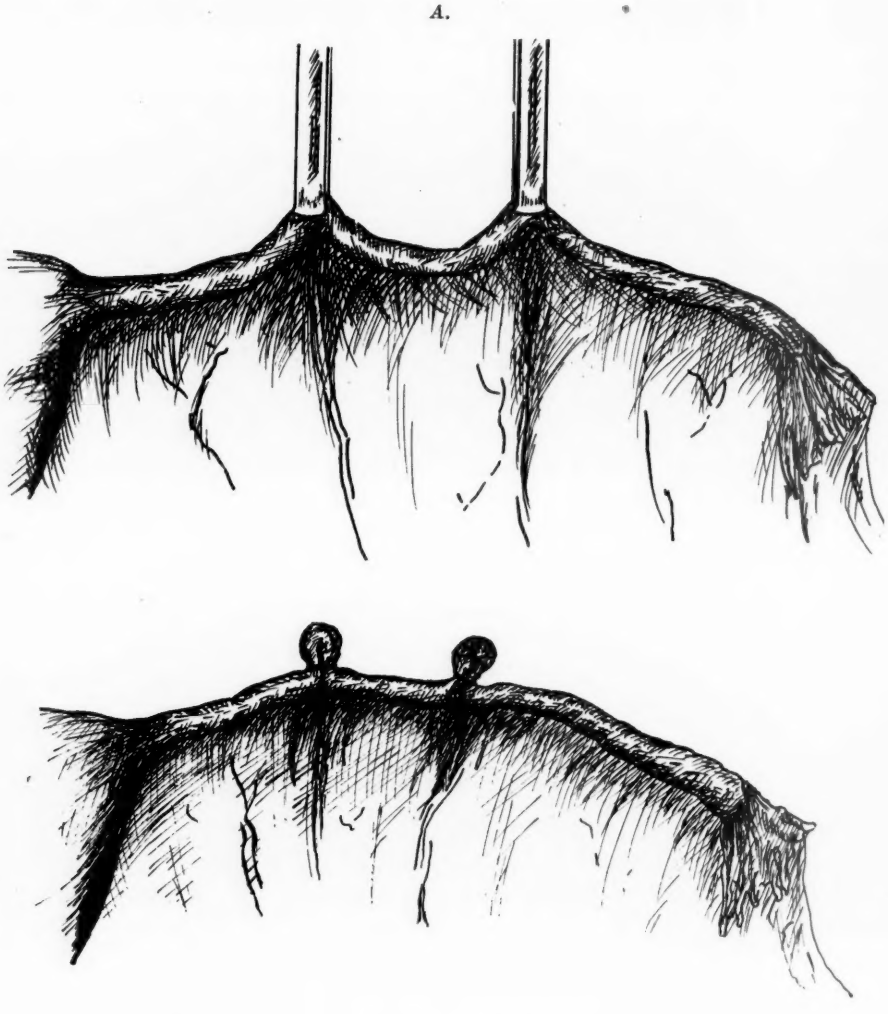
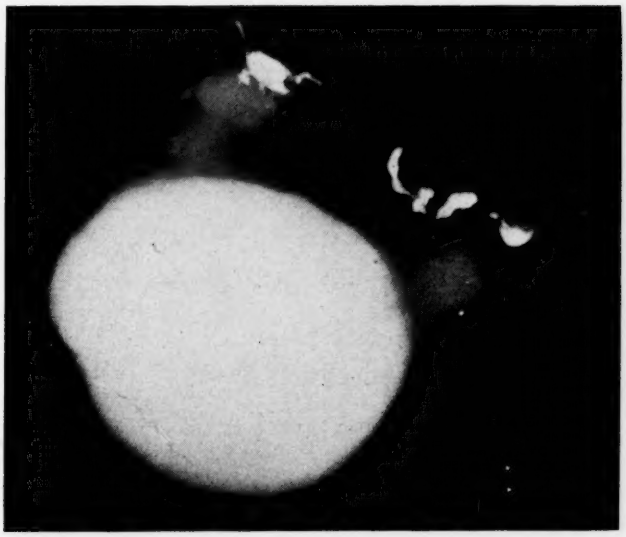


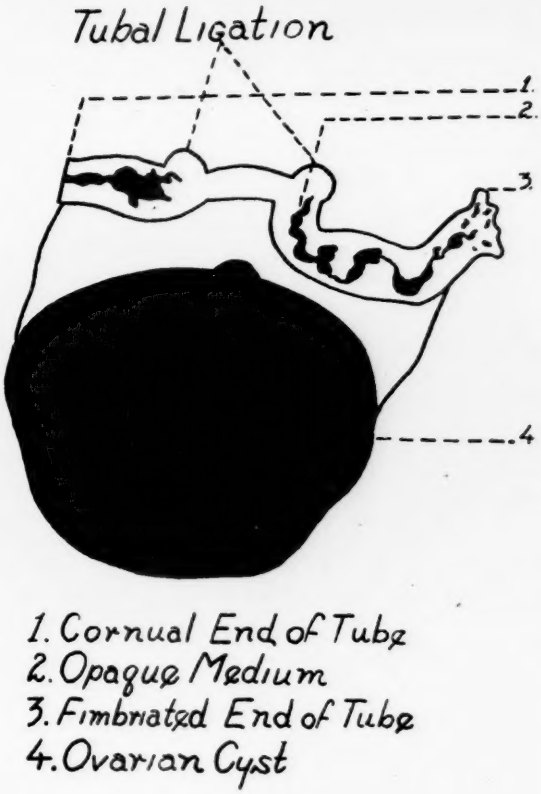
Fig. 1.—Diagrammatic illustration of method of double tubal ligation for sterilization.

The patient was again seen on Jan. 15, 1945, complaining of amenorrhea, and she was found to be pregnant. The biological test was positive. Contrary to our advice, the patient obtained an induced abortion on Feb. 3, 1945. Subsequently, she returned to us for repair of the rectovaginal fistula, and requested that she be sterilized once more.

On May 18, 1945, she was operated on by one of us (I. F. S.) at Michael Reese Hospital. Because of the need for vaginal plastic repair and closure of the rectovaginal fistula, it was decided to approach the left tube through the

A.





B.

Fig. 2, *A.* and *B.*—Opaque medium instilled into both ends of excised tube showing adequate sterilization by double ligation.

anterior cul-de-sac. Technical difficulties arose in attempting to reach the tube for sterilization and, therefore, vaginal hysterectomy and left salpingo-oophorectomy were performed. The following is a description of the operation:

A. *B.*

Fig. 3.—Two cross sections of tubal lumen visualized. *A.* Complete obliteration by fibrosis after tubal ligation. *B.* Patent lumen in right uterine horn eleven years after salpingo-oophorectomy.

Under low spinal anesthesia (Pontocaine) the cervix was brought down and an attempt was made to separate the bladder from the uterus. In so doing, the bladder, which was extremely adherent (after two low cesarean operations) was inadvertently opened. The bladder was then completely mobilized from the uterus by scissors dissection and the laceration repaired with three rows of fine catgut. The anterior cul-de-sac was then opened and the uterus and left adnexa were extirpated. The entire left adnexa were removed because of an ovarian cyst measuring about 3 by 4 cm. with adhesions between the tube and ovary (the right adnexa had been removed eleven years previously). The vaginal vault was then suspended by corner stitches placed in the round and uterosacral ligaments. The peritoneum was closed with fine catgut and the vaginal vault closure completed with interrupted circle stitches of No. 1 catgut, leaving a small wick of sulfathiazole gauze draining the subvesical space. For repair of the rectovaginal fistula, a V-shaped flap was removed from the posterior vaginal wall, the region of the levator ani muscles exposed, and the repair carried out, bringing the small fistulous opening toward the perineum. The fistulous tract was excised and the tissue closed over it in layers. The perineal skin was approximated with interrupted plain catgut No. 0 stitches. A retention catheter was left in the bladder.

The patient made an uneventful recovery, completely relieved of both her old rectovaginal fistula, the recent (operative) vesicovaginal fistula, and she was finally adequately sterilized.

We had assumed that this was an instance of a failure of tubal ligation, the first we had encountered by the method of double ligation which we have described and illustrated. X-ray of the excised tube and pathologic examination of the removed organs revealed the following: the left tube when tested with opaque medium (lipiodol, Fig. 2) was found to be nonpatent. Upon injecting the uterine end of the excised tube with the opaque medium, it stopped at the first ligation. Injection into the fimbriated end was likewise found to be limited by the second ligated loop. Hence the tubal sterilization had been entirely successful. Furthermore, serial sections of the left tube confirmed the fact that continuity of the lumen was interrupted by the formation of fibrous tissue so that sterilization performed at the time of the second cesarean operation was competent. (Fig. 3*A*.)

With the double obstruction of the left tube clearly proved, the only possible way that an ovum could enter the uterus would be through the right cornu, the site of the previous right salpingo-oophorectomy. Therefore, serial sections were taken through the right cornu of the uterus. The interstitial portion of the right tube proved to be patulous. (Fig. 3*B*.)

The mechanism of conception in this case was obviously by means of external migration of the ovum. The right ovary and tube had been removed previously and the left tube had been successfully ligated. Therefore, the ovum, either before or after fertilization, entered the uterine cavity through the patent interstitial portion of the right tube.

Reference

Polak, J. O.: Am. J. Obst. & Dis. Wom. & Child. **61**: 676, 1910.

ENDOMETRIOSIS OF EPISIOTOMY SCAR*

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ENDOMETRIOSIS is by no means a rare condition, and the sites in which endometrial tissue can implant itself are numerous: the ovaries, bowel, appendix, abdominal scars, etc. However, endometriosis in the perineum is extremely unusual. Schickelé,[1] in 1923, reported on the first case of perineal endometriosis. Neuwiller[2] in 1926 and Prager[2] in 1932 reported cases of perineal endometriosis following a perineal laceration resulting from a delivery. In 1933, Maliphant[2] reported a case following a colpoperineorrhaphy. Weiss and Synephia[2] in 1934 reported two additional cases of perineal endometrioma. In 1941, Jessing[3] reported a case following a curettage and operation for prolapse. Micholitsch[2] reported a case of endometriosis in an episiotomy scar appearing several weeks following a forceps application.

The case to be presented we believe to be the first one reported following a normal spontaneous delivery.

Mrs. L. W., a 23-year-old Negro female, hospital number 45-36684, was admitted to the Cook County Hospital, Sept. 4, 1945. She was a para i, gravida ii. In 1940, the patient had a spontaneous abortion of a four and one-half-month fetus. In 1941 she had a normal spontaneous delivery of a full-term infant weighing 7 pounds 2 ounces, at which time a left mediolateral episiotomy was performed. It was repaired in layers using interrupted black silk sutures for the skin. Her postpartum course was uneventful and she was discharged on the tenth postpartum day in good condition.

On her present admission to the hospital she complained of marked pain and swelling in the region of her episiotomy scar. The pain and swelling recurred every month with the onset of her menstrual period, and would be relieved when the flow stopped. She had noticed this particularly in the last year but she had similar discomfort since about five to six months after her delivery.

On examination of the perineum there was evidence of a healed left mediolateral episiotomy scar. A hard mass was palpable the whole length of the scar. It measured 5 by 2 cm., was attached to the skin and underlying tissue. It was not particularly tender. A diagnosis of endometrioma was made.

On Sept. 11, 1945, the old scar and the mass were completely excised. The mass was found to extend down to the levator fascia.

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*Presented before the Chicago Gynecological Society, March 21, 1947.

Fig. 1.—Section of the excised episiotomy scar.

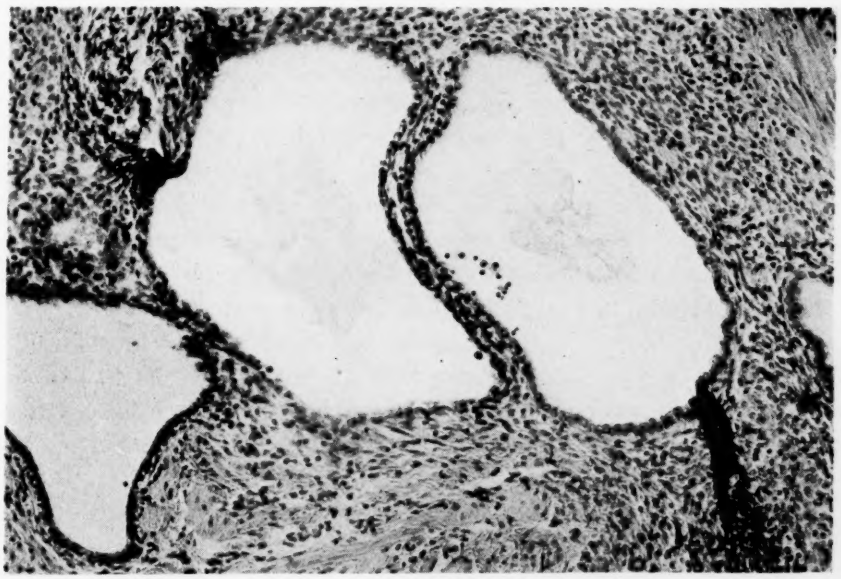

Fig. 2.—Another section of the excised episiotomy scar.

Grossly, many blue pinpoint nodules were seen. Microscopic examination of this tissue showed endometrial glands and stroma. The diagnosis of endometriosis occurring in an episiotomy scar was confirmed.

Follow-up observation revealed the wound was well healed, and the patient had no further complaints of pain or swelling.

References

1. Schickelé: Bull. et Mem. de la Soc. Anat. de Paris **20**: 601, 1923.
2. Weiss, A. C., and Synephia, M.: Ann. d'anat. path. **15**: 745, 1934.
3. Jessing, A.: Acta Obst. et Gynec. Scandinav. **21**: 225, 1941.

PENTOTHAL SODIUM ANESTHESIA FOR CESAREAN SECTIONS

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THERE are many articles in the literature relating to the use of Pentothal sodium in obstetrics, but few of them more than mention its use as the anesthetic for patients undergoing cesarean section.

Kassebohm and Schreiber[1] state that they have never been able to perform cesarean sections with either Pentothal or Evipal. Since publishing their paper in 1938, they have changed their views and find that they can use Pentothal if they have a competent, well-trained anesthetist to administer the anesthesia. Hellman, Shettles, Manahan, and Eastman[2] list its use in 114 cases and state, "It is quite adequate for cesarean sections."

At Grace Unit of Grace-New Haven Community Hospital, from 1942 to 1946, there were 492 cesarean sections performed using Pentothal as the sole anesthetic agent until after delivery. In practically all of these cases, it was the main anesthetic agent throughout the operation, supplemented with a mixture of equal quantities of oxygen and nitrous oxide after delivery of the child. The work is still going on, and it is hoped that a subsequent paper may include these later cases.

As was customary in 1942, this series was started using a 5 per cent solution of Pentothal, but in 1943 this was changed to a 2.5 per cent solution, and this is the concentration which has been used since. It is interesting to note that the total dosage of the 5 per cent solution in these early cases was much larger than is our present total dosage, sometimes as much as 2.5 Gm. being used. It was not supplemented, however, with oxygen and nitrous oxide. This serves as a good example, I believe, of the advantage of using some supplementary anesthetic to cut down the total dosage of Pentothal. No doubt some of the decrease is also due to an increased skill in administration which comes with experience in a large number of cases.

It seems to me that, from the viewpoint of the mother, there is a definite advantage in this form of anesthesia. Since she is asleep, she is spared the apprehension which would be experienced if, for any reason, the baby should not cry promptly. Induction is very quick, quiet, and pleasant. Unconsciousness is attained within twenty to thirty seconds, and, in most patients, if the surgeon is not too timid about making the skin incision even though there is some pain reaction, the operation may proceed within one to one and one-half minutes after the anesthesia started. Incidentally, I have never had a patient who has remembered any pain of incision even though many of them react when the skin incision is made.

The anesthesia is so pleasant for the patient that most of them ask for it now when seen by the anesthetist before operation. In fact, if the patient has to have a subsequent operation for some other condition for which it is felt that Pentothal is not the anesthetic of choice, it is very difficult to convince her of this. This may be regarded as a disadvantage in some patients.

As pointed out by Hellman,[2] Pentothal passes through the placenta, reaching equal concentration in fetal and maternal blood within ten to twelve minutes. There is apparently a period of five to eight minutes, however, after starting the anesthesia, during which the amount of the drug reaching the fetus is very small. This point should be borne in mind by the operator doing an occasional cesarean, I believe, since the margin of safety for the fetus may be too narrow in his hands.

Since the average time from the start of anesthesia to the delivery of the baby was 8.83 minutes, we were well within the safety period. This includes the patients operated upon by the resident staff and the occasional one by the general surgeon, which brings the average time up considerably. Another factor which raises it, is the inclusion in this series of a fair number of Waters' sections, although most of the operations were of the low-flap type. In most cases done by the attendings on the obstetric service, the fetus is delivered in between four and six minutes after the start of anesthesia.

In this series, there were 48 mothers, or 10 per cent, who had either nausea or nausea and vomiting postoperatively. Practically all of these had only nausea, and the occasional ones who did vomit usually did so only once or twice. The average time for the mother to react from the anesthetic was figured as 28.7 minutes. Actually this is too high, however, since the time was figured from the time that the operation was finished to the time the patient first required something for the relief of postoperative pain, except for those who were reacting when they left the operating room. There were 106 of these, which is 21.5 per cent.

There were no maternal deaths. Thirteen, or 2.7 per cent, of them had atelectasis, which, in every case but one, was mild. Since many of these patients who were operated upon as emergencies had some respiratory infections, and others had had a recent meal, it is surprising to see that this figure is not higher. It is not our practice to operate upon patients who have an upper respiratory infection, but when a patient requiring a cesarean section goes into labor, we have no choice.

There were 15 fetal deaths or 3 per cent. These were patients in whom the fetal heart was heard prior to induction of anesthesia. The causes of death in these 15 infants are listed in Table I.

TABLE I. FETAL DEATHS—FETAL HEART HEARD PRIOR TO THE INDUCTION OF ANESTHESIA

Prematurity	7
Erythroblastosis	1
Atelectasis	5
Congenital heart disease plus atelectasis	1
Cerebral anoxemia	1

There were only five of these deaths in which it is felt that the anesthetic may have had an adverse effect on the fetus. All of these were cases in which, due to a prolonged induction time or too slow delivery of the baby or both, we

went over the safe period. No doubt the Pentothal was of about equal concentration in both maternal and fetal blood.

It is felt that some of these infants might have been revived had more expert resuscitation been available. Too often this art is left to the family physician or an inexperienced intern. This was especially true during the war years, which is the period covered in this report. Adequate, well-trained help was scarce during that period. Those to whom this important task was assigned did their best, but, unfortunately, they had not had sufficient experience in the use of the resuscitator.

There is also more to the proper sucking-out of the pharynx in a newborn infant than in an adult. Too often some well-meaning person, in attempting this procedure, will put a large finger down the infant's throat in an attempt to get the suction tip in close proximity to the larynx. Suction is doubtless fairly efficient, but the finger is filling the entire pharynx and thus obstructing the first feeble attempts of the infant to inhale. My opinion is that this important procedure should be intrusted to that person who is best trained in its use.

There were 331 or 70 per cent of the infants who cried spontaneously. The remaining 139 or 30 per cent were resuscitated by means of suction plus oxygen under slight pressure. There were 27, or 5.7 per cent, who required oxygen after admission to the nursery. All of these were premature with the exception of those who had some congenital anomaly such as those listed in Table I.

Technique

The night before operation on an elective-cesarean patient, she is examined by the medical anesthetist, and Nembutal—grains 1½, is given. One hour before operation, she is given atropine, grain 1/150 by hypodermic.

Upon arrival in the operating room, the patient is catheterized and placed in position on the operating table. Her pulse, blood pressure, and respirations are checked by the anesthetist. The abdomen is painted and draped.

As the last drapes are being put on, the Pentothal is started, 2 to 3 c.c., followed by about a thirty-second wait to watch the effect. The Pentothal injection is then continued slowly but steadily while the depth of the respirations, the lid reflex, and movement of the eyeballs are carefully watched. As the anesthesia approaches the third plane, the surgeon tests the reaction of the patient to pain by pinching the skin with an Allis clamp. If there is only slight reaction, the incision is made. Oxygen by mask connected to the anesthesia machine is started at the same time as the operation, or before, if there is a lag in reaching the desired depth of anesthesia. Usually it requires between 400 and 500 mg. of 2.5 per cent Pentothal before the operation can be started. Occasionally, a patient may require between 500 mg. and 1 Gm. As soon as the infant is delivered, 1 c.c. of Ergotrate is given intravenously to the mother and either nitrous oxide is added to the oxygen in an equal quantity, or, if it seems more desirable, the Pentothal may be discontinued and the operation finished with cyclopropane and oxygen. We are rather more likely to do the latter if the patient has required over 500 mg. of Pentothal for delivery of the baby.

Conclusions

It is not claimed that this is the only safe anesthetic or even the safest anesthetic for this operation. In our hands, however, we feel that it has definite advantages in most patients.

1. I still maintain, however, that the choice of anesthetic for such cases should be based on the following facts:

1. Condition of the patient.

2. Skill and training of the anesthetist.
3. Operative skill and experience of the surgeon.

We must never forget, in cesarean sections, that we have two or more lives to consider, instead of the one involved in other surgical operations.

Summary

The use of Pentothal sodium as the anesthetic in a consecutive series of 492 cesarean sections is reported. There were no maternal deaths. The incidence of nausea and vomiting was small. The 2.7 per cent atelectasis may at first thought seem high, but when it is considered that many of these operations were done as emergencies, it takes on a much less serious aspect.

There were 15 fetal deaths, only 5 of which may have been due in any respect to the anesthesia.

References

1. Kassebohm, F. A., and Schreiber, M. J.: Am. J. Surg. 40: 381, 1938.
2. Hellman, L. M., Shettles, L. B., Manahan, C. P., and Eastman, N. J.: Am. J. Obst. & Gynec. 48: 851-860, 1944.

COMBINED LOCAL INFILTRATION ANESTHESIA AND PENTOTHAL SODIUM ANESTHESIA IN CESAREAN SECTIONS

A Preliminary Report

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THE use of local infiltration anesthesia in any surgical procedure has decreased the dangers associated with a general anesthetic by decreasing the effects of anesthetic agents on the vital nerve centers. In abdominal surgery, local infiltration anesthesia in conjunction with general anesthesia has been useful in assuring good muscular relaxation. General anesthesia in cesarean sections has long been a disputed question because of fetal narcosis.

There is a certain amount of apprehension caused in the patient when local infiltration anesthesia is used alone in abdominal surgery or in cesarean sections. This has been minimized in many instances by combining local anesthesia with analgesia such as nitrous oxide and oxygen or by using morphine sulfate and scopolamine hydrobromide but, again, in cesarean sections fetal narcosis may be produced. If the operative procedure should take longer than contemplated, apprehension again appears, accompanied with some discomfort to the patient.

Pentothal has become a favorite anesthetic in general surgery but in cesarean sections its disadvantages are evident because of the narcotic effect on the infant, necessity for rapid delivery, and its limitations to the elective type of cesarean section only.

We have combined local anesthesia and nitrous oxide analgesia with intravenous Pentothal sodium. Pentothal sodium was chosen because of its rapid and smooth induction and its relative safety as an anesthetic agent when used properly.

In obstetrics there are such complications as placenta previa, the toxemias, fetal distress, or cephalopelvic disproportion, in the presence of an upper respiratory infection in which a general anesthetic may be harmful to both the mother and the infant. With these complications and the relative safety of both the mother and the infant in mind, we have used a simplified technique of local infiltration anesthesia associated with intravenous Pentothal sodium.

Technique

Tissue trauma and haste must be avoided for a successful result.

A 1 per cent solution of Novocaine, without Adrenalin hydrochloride, is used throughout the procedure. It may be necessary to use nitrous oxide

analgesia while carrying out the technique to allay the apprehension which may occur in the patient. The use of 50 to 100 mg. of Demerol preoperatively has been very helpful and also less depressing to the infant.

1. The operative site is directly infiltrated with Novocaine; this includes infiltration of the dermis. An initial wheal is made using a 26 gauge needle. This is preferably made at a point midway in the contemplated length of the incision. The entire infiltration may be successfully made through this point by using a 4 inch, 20 gauge needle and constantly moving the needle while infiltrating the dermis.

2. The subcutaneous tissues are then infiltrated down to the fascia.

3. Perpendicular punctures of the abdomen are then made penetrating the fascia. These punctures are approximately 1 inch to 1½ inches apart and the fascia and underlying musculature are infiltrated with Novocaine.

4. After a few minutes' wait, the skin is incised down to the fascia. Hemostasis is assured and all bleeding points are ligated. During this delay the fascia and the muscular tissue directly beneath the fascia become anesthetized.

5. The fascia is then incised. This is best carried out by using the scalpel. This prevents the pressure and tearing effect caused by using scissors.

6. The recti muscles are infiltrated laterally to the outer borders of their respective sheaths. A 4 inch, 20 gauge needle is used; infiltration points are approximately ¾ inch apart and the needle is moved constantly during the infiltration. By following this procedure, both the anterior and posterior branches of the thoracic nerves which supply the anterior abdominal wall are anesthetized. The underlying preperitoneal tissues are also anesthetized.

7. The edges of the abdominal incision are draped with sterile towels and the peritoneum is directly infiltrated with Novocaine. This is incised and the preperitoneal tissues laterally, including the posterior portion of the rectus sheath, are again infiltrated using the technique as described above. Relaxation is assured and the uterine wall is exposed. No packs are inserted into the abdominal cavity to wall off the uterine incision. Retractors may be used if found necessary.

8. The uterus is centered or adequately exposed, Pentothal anesthesia is started, and the uterus is then opened. In low cervical cesarean sections the Pentothal anesthesia is started following infiltration and dissection of the vesical fold.

Local infiltration of Novocaine and intravenous Pentothal sodium anesthesia were used in a group of 40 patients. There were 16 primiparas and 24 multiparas.

The indications for cesarean section were as follows:

Bicornate uterus, elderly primipara	1
Cephalopelvic disproportion	16
Diabetes mellitus	2
Pulmonary tuberculosis	1
Toxemia of pregnancy	2
Fetal distress	2
Previous cesarean section	7
Previous myomectomy, no viable infants	1
Placenta previa	1
Placenta previa, multiple pregnancy	1
Surface carcinoma of cervix	1
Inertial labor	2
Previous extensive vaginal repair	2
Rheumatic heart disease	1

There were twenty-seven classical cesarean sections; this included four cesareans with a high uterine incision. There were thirteen low cervical cesarean sections. An incisional hernia was repaired in one case. In five cesareans, lysis of adhesions and appendectomies were performed. An ovarian cyst was removed during one laparotomy.

The length of time from the beginning of the infiltration of the Novocaine and the extraction of the child varied from nine to thirty minutes; the majority of the infants were delivered within fifteen minutes. This variation in time was due to the degree of sensitivity to pain found in some of the patients.

The average amount of Pentothal used was 12.4 grains; 5 grains were used in one case and the maximum was 30 grains. The majority of the patients required only 11 grains of Pentothal sodium. Intravenous Pentothal sodium was given after completion of a classical uterine incision in 6 patients. In 9 patients the time interval was one minute before the birth of the child. Intravenous Pentothal was given two minutes before the birth of the infant in 12 patients. In 7 patients the time interval varied from three to six minutes. In 2 patients the time interval was seven minutes from the time the Pentothal was given to the birth of the infant.

Atropine sulfate, gr. $\frac{1}{150}$ (0.4 mg.), was the only premedication in 17 patients. Demerol with atropine sulfate was given preoperatively in 22 patients; 2 patients received 50 mg. of Demerol; 4 patients received 75 mg. of Demerol and the remaining 15 patients received 100 mg. of Demerol. One patient received morphine sulfate, gr. $\frac{1}{6}$ (11 mg.), and atropine sulfate preoperatively. Nitrous oxide analgesia in small amounts with continuous oxygen was used during the operation with all the patients.

The length of time from the first infiltration of the operative site to the completion of the operation varied from thirty to seventy-four minutes. The average time was forty-seven minutes.

Complications

A mild laryngospasm occurred in one patient. This patient was a gravida iii, para ii. Her first pregnancy terminated spontaneously. The second pregnancy was terminated by a cesarean section because of a severe pre-eclampsia. Her third pregnancy was terminated by a classical cesarean section and the fallopian tubes were ligated by the Madlener technique. The patient was administered 100 mg. of Demerol and $\frac{1}{150}$ grain (0.4 mg.) atropine sulfate preoperatively. The length of time between infiltration of the abdominal wall and the birth of a viable infant was seventeen minutes. The infant was delivered two minutes after the injection of Pentothal sodium. Three minutes later a mild laryngospasm occurred followed by an excessive amount of vomiting. A total of 25 grains of Pentothal sodium was used during the operation. The postoperative course was uneventful.

Results

1. There was no fetal or maternal mortality in this series of patients.

2. There was delayed fetal respiration in two cases. In these cases, seven minutes elapsed from the beginning of the Pentothal anesthesia to completion of the delivery of the infant. All of the remaining infants breathed spontaneously. Thirty per cent of the babies began crying as soon as the head was delivered through the opening in the uterus.

3. As far as it is possible to determine with this small series, Demerol preoperatively had no effect on the infant. Its analgesic action to the patient was gratifying.

4. Pentothal sodium given immediately before the incision in the uterus allows for unobstructed and rapid delivery of the infant with no effect to the infant and no discomfort to the patient.

5. The immediate postoperative condition of the patients was satisfactory. There was no abnormal nausea or vomiting. Actually, the postoperative reaction of the patient seemed to be superior to that with other forms of inhalation anesthesia. This was augmented by giving the patients 100 mg. of Demerol immediately upon showing signs of reacting from the anesthetic.

Summary

Carefully combined local infiltration anesthesia and Pentothal anesthesia give excellent results in cesarean section (both mother and infant) providing undue haste and tissue trauma are eliminated.

RECTAL HEMORRHAGE FOLLOWING IRRADIATION FOR CARCINOMA OF CERVIX

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LATE intestinal complications following irradiation for pelvic malignancy are recognized and frequently anticipated. There are degrees of damage to the distal colon, varying from the mildest type causing a simple proctitis, through stages of destruction terminating in atrophy, stenosis, or perforation. These changes often are on the basis of obliterative endarteritis or telangiectasia. Rectal hemorrhage frequently responds to medical treatment or to colostomy. Relatively few cases require colostomy, but when necessary, it is usually entirely effective in relieving the condition.[1] We report a case of severe, intractable rectal hemorrhage following radiation therapy for recurrent carcinoma of the uterine cervix which necessitated not only colostomy, but even excision of the distal sigmoid and rectum to stop the hemorrhage. We have not found a similar case reported.

In addition, thirteen months later, this patient developed a primary carcinoma of the ascending colon which was resected, and the patient remains in normal health seven years later, without evidence of recurrence of either neoplasm.

Mrs. I. H., aged 47 years, weight 132 pounds, and the mother of one child, gave a history of having "a growth removed from the uterus" in April, 1935. In April, 1936, she had a uterine hemorrhage. Her physician stated the pathology report showed no carcinoma, but she received a small exposure (amount not given) of radium in the cervix and fundus. In March, 1937, she had recurrence of vaginal bleeding and a biopsy showed carcinoma of the cervix. She had more radium, reported to be a 50 mg. focus for forty-eight hours, or 2,400 mg. hr. She was then referred to our clinic for x-ray treatment. She received a series of high voltage (200 kv. 0.5 mm. Cu) x-ray treatments to a total of 1,600 r. (measured in air) to each of four pelvic portals 12 by 17 cm. in size, over a period of sixteen days. This was given at the daily rate of 200 r. to each of two portals, alternating front and back. Biopsy after the x-ray series showed no neoplastic cells present.

In September, 1937, she complained of a yellowish vaginal discharge. A biopsy of the cervix showed papillary adenocarcinoma. She was treated with radium consisting of two 40 mg. capsules (with 1 mm. platinum filtration) tandem in cervix and fundus and four 10 mg. needles (0.5 mm. platinum) in the parametria for thirty hours, giving a total of 3,600 mg. hr. This was followed in ten days by x-ray treatment with the same technique as before, totalling 1,400 r. to each of four portals over a period of fourteen days.

In April, 1938, there was moderate bleeding from the rectum. In September, this bleeding was more profuse and she was admitted to the hospital Oct. 4, 1938. The red blood cell count dropped steadily from 3,020,000 to 2,450,000 even though she had two transfusions. A colostomy was performed on Nov. 4, 1938. Following this the bleeding continued and the red blood cell count fell to 1,450,000. Since conservative treatment failed, it was then deemed advisable to do a resection of the sigmoid and rectum. After several transfusions, this was

done on Jan. 4, 1939. The pathology report of excised bowel was as follows: "A section of sigmoid and adjacent descending colon was received. The entire specimen measures 23 cm. in length and has an average circumference of 4 to 4½ cm. The distal 6 cm. of the bowel is indurated. This induration involves not only the mucosa and submucosa but also the appendices epiploicae. The mucosa in this segment presents a fiery red, finely granular appearance and is definitely depressed from the remaining smooth, velvety, pink mucosa. The remainder is normal in consistency. The wall in the indurated area is rather thicker than average and the mucosa here has lost its normal haustrations. On careful examination of the mucosa, a number of small diverticula can be demonstrated in its proximal one-third. The lower one-third possesses a smooth mucosa that shows a great number of minute, distended blood vessels.

"*Microscopic:* Section through the granular portion of mucosa of the distal segment exhibits a fibrous type of granulation tissue in which a small number of isolated, large cells are found. These cells vary in size and shape, possess gigantic, almost black-staining nuclei and occasionally an acidophilic nucleolus about 7 microns in diameter. The mucosa here is completely absent. The granulation tissue is heavily infiltrated by inflammatory cells of all types. The muscularis is essentially normal. The serosa, in this as well as sections remade from this area, show fibrosis, foci of monocytic infiltration and foreign-body, giant-cell reaction. The mucosa elsewhere shows no striking change.

"*Diagnosis:* Metastatic carcinoma, undifferentiated in submucosa of colon. Extensive chronic ulceration of colon with cicatrization of submucosa."—*Dr. Paul Gross.*

The postoperative course was complicated by wound infection and thrombophlebitis of the left leg. She was discharged from the hospital Feb. 25, 1939, with a red blood cell count of 3,200,000 and a weight of 100 pounds.

She gained steadily throughout that year, but in January, 1940, a mass appeared in the region of the right colon which produced no symptoms. X-ray examination of the colon showed a constriction in the ascending portion suggestive of a new growth. Operation Jan. 30, 1940, consisted of resection of the ascending colon and hepatic flexure with lateral anastomosis of the cecum to the transverse colon. Histologic examination showed "undifferentiated carcinoma involving large bowel." She had an uneventful convalescence and gained steadily in weight. One year later, in January, 1941, her weight was 144 pounds. Her only complaint was frequent urination, due to a bladder capacity of 7 ounces. This condition persists to the present time.

The years 1942 and 1943 were uneventful.

In July, 1944, the patient had an attack starting with chills followed by high fever, and accompanied by an erysipelas-like eruption of the skin of the vulva, mons, and upper thigh. To date, April, 1947, she has had ten or twelve of these attacks. Sulfonamides brought the temperature to normal in two or three days, but in the past two attacks recovery was much quicker when 300,000 units of penicillin in oil and wax were given at the onset. Despite this complication the patient considers herself in excellent health.

Comment

This patient made remarkable recoveries from three potentially fatal conditions, namely, recurrent carcinoma of the uterine cervix, severe, intractable rectal hemorrhage due to irradiation and metastatic carcinoma, and a second primary carcinoma of the ascending colon.

The rectum was damaged from the large amount of irradiation required to control the cervical lesion. This type of rectal inflammation resulted in bleeding so prolonged and profuse, despite every known means of treatment, that life was endangered. The bleeding was from a smooth, granular surface without slough or erosion of sizeable vessels. The pathologic findings were those

of fibrosis with the presence of neoplastic cells. This may have produced hemorrhage by preventing the arterioles from contracting and was corrected only by resection of the bowel, thus permitting the long survival.

Incidentally, it is not often that microscopic changes of the entire bowel wall can be studied as in this case, because ordinarily only small pieces are obtained as biopsy specimens.

The lesion of the ascending colon probably was not a neoplastic extension or metastasis, because an x-ray examination fifteen months before showed that portion of the bowel to be normal. Even though a total of approximately 50 per cent of the colon was resected, the colostomy functions well and requires little attention.

The intermittent attacks of erysipeloid eruption of the pubic and perineal regions are probably related to partial lymphatic blockage which favors a low-grade, chronic inflammation. This is similar to the phenomenon in an edematous upper extremity following radical mastectomy. The etiology is unknown but the response to sulfonamides or penicillin is prompt.

The small capacity of the urinary bladder, in the absence of cystoscopic evidence of interstitial cystitis, is probably due to the fibrosis and contraction as a result of the extensive irradiation and surgery.

Summary

A 47-year-old woman who was treated twice with radium, followed by two pelvic x-ray series, for carcinoma of the uterine cervix, one year later developed severe rectal bleeding which required resection of the terminal large bowel. About a year after that, she developed a clinically silent primary carcinoma of the ascending colon which was treated surgically. Ten years after the cervical carcinoma and seven years after the cancer of the colon, she continues in excellent health without recurrence of either neoplasm.

Reference

1. Todd, T. F.: Surg., Gynec. & Obst. 67: 617-631, 1938.

CERVICAL CANCER WITH METASTASIS TO BREAST

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MAMMARY metastasis from carcinoma of the uterine cervix is either exceedingly rare or it has been overlooked. The literature contains several reports of cases in which malignant tumors appeared independently in the breast and cervix of the same patient (Smith and Bartlett, 1929; Cordua, 1929, 1936; Taylor, 1931; Schreiner and Wehr, 1934; Hellendall, 1935; Fernandez-Colmeiro, 1946; Taylor and Guyer, 1946). A case has also been recorded in which a probable metastasis to the cervix occurred in a woman with a primary mammary lesion (Esch, 1929). We have been able to find references to only four cases, however, of primary cervical cancer associated with metastatic tumor in the breast. Three of these were mentioned briefly by C. Schroeder (1887) in a review of the previously published papers of six other authors. The fourth appeared in a summary of the material in the Pathological Institute at Kiel between 1914 and 1918 (Petzold, 1922). In none was the case described nor were photographs shown.

More recent studies of the sites of metastases from cervical carcinoma fail to list the breast among the organs affected. Among these studies are Meigs' report (1934) of 396 cervical cancers, and Gricouroff's analysis (1942) of 2,076 cases in the Curie Radium Institute. The following case is reported because it represents the first proved instance of metastasis to the breast from one of the commonest of all human tumors.

Mrs. A. L. was a 49-year-old white nulliparous divorcee. Her past history included a spontaneous abortion in 1915, appendectomy in 1928, tuberculosis with eight months' hospitalization in a sanitarium in 1930, and a membership in Alcoholics Anonymous. She complained of intermenstrual spotting in September, 1945, at which time biopsy of the cervix revealed epidermoid carcinoma (Fig. 1). A course of sixteen deep x-ray treatments was given between Oct. 1 and Nov. 5, 1945, the patient receiving 1,500 roentgen units to each of four pelvic portals. On Nov. 4, 1945, 140 mg. of radium was applied in and against the cervix for a total dose of 3,000 mg. hours. The patient was hospitalized again from March 5 to 15, 1946, because of pelvic pain and dysuria. Roentgenogram of the chest and intravenous pyelogram were negative. A mild cystitis responded to treatment with sulfadiazine and penicillin. She was readmitted on May 13, 1946, because of a sudden profuse vaginal hemorrhage, for which she was treated with vaginal packing and blood transfusion. Her final admission to Roosevelt Hospital was Nov. 15, to Dec. 14, 1946, when she complained of severe low back pain. The patient had lost much weight and appeared chronically ill. General physical examination was essentially negative, save for enlarged left supraclavicular lymph nodes and a small firm nodule, about 1 cm. in diameter, in the upper outer quadrant of the left breast. The tumor was superficial, but not attached to the skin. Pelvic examination revealed no evidence of the previously existent cervical tumor. Roentgenograms of the skull showed two areas of decreased density which were interpreted as metastases.

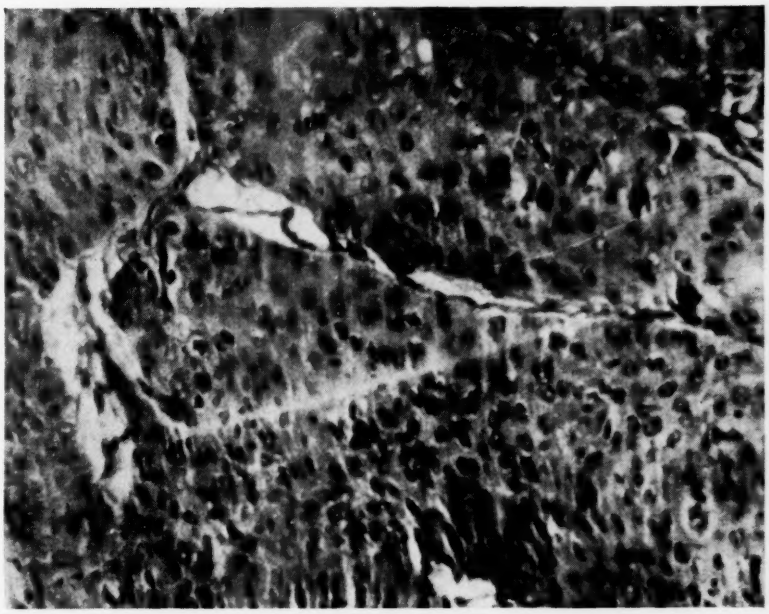

Fig. 1.—Cervical carcinoma.

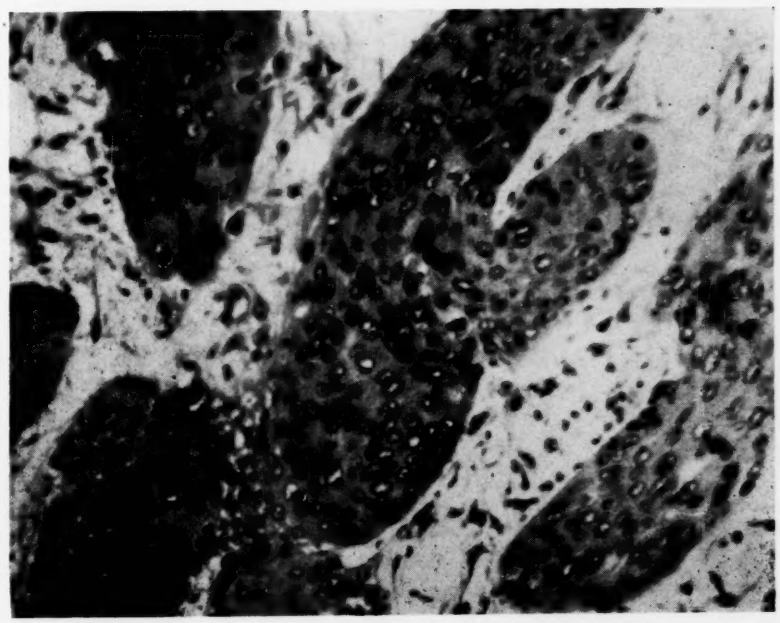

Fig. 2.—Metastasis in left breast.

Biopsy of the nodule in the left breast was performed on Dec. 6, 1946. Pathologic report was "metastatic epidermoid carcinoma in the breast" (Fig. 2). The histologic appearance of this tumor was identical to that of the original cervical biopsy. Unsuccessful efforts were made to control the patient's back pain with large doses of testosterone propionate (50 mg. daily) and with cobra venom. Requiring constant narcosis, she was transferred to a home for terminal care, where she died about Feb. 1, 1947.

Metastatic tumors of the breast are rare. Dawson was able to collect only ten cases from the literature in 1936 and added one of her own, a gastric carcinoma. This, then, represents the twelfth reported case of metastatic carcinoma in the breast. The infrequency of carcinomatous metastasis to this organ was responsible in part for Virchow's generalization (1863), long since disproved, that most organs which show a strong disposition to the development of primary malignant tumors are seldom the site of a secondary tumor.

References

Cordua, R.: Zentralbl. f. Gynäk. **53**: 1711-1715, 1929.
Cordua, R.: Zentralbl. f. Gynäk. **60**: 322, 1936.
Dawson, E. K.: J. Path. & Bact. **43**: 53-60, 1936.
Esch: Zentralbl. f. Gynäk. **56**: 556-558, 1929.
Fernandez-Colmeiro, J. M.: Bull. assoc. franç. p. l'étude du cancer **33**: 16-35, 1946.
Gricouroff, G.: Bull. assoc. franç. p. l'étude du cancer **30**: 90-117, 1942.
Hellendall, H.: Zentralbl. f. Gynäk. **59**: 2554-2560, 1935.
Hellendall, H. Nochmals: Zentralbl. f. Gynäk. **61**: 1642-1645, 1937.
Meigs, J. V.: Tumors of the Female Pelvic Organs, New York, 1934, The Macmillan Co.
Petzold, H.: Ztschr. f. Krebsforsch. **19**: 245-262, 1922.
Schreiner, B. F., and Wehr, W. H.: Am. J. Cancer **20**: 418-424, 1934.
Schroeder, C.: Handbuch der Krankheiten der Weiblichen Geschlechtsorgane, ed. 8, Leipzig, 1887, pp. 292-293. F. C. W. Vogel.
Smith, G. V. S., and Bartlett, M. K.: Surg., Gynec. & Obst. **48**: 314-320, 1929.
Taylor, H. C., Jr.: Am. J. Cancer **15**: 277-279, 1931.
Taylor, H. C., Jr., and Guyer, H.: Am. J. Obst. & Gynec. **52**: 451-455, 1946.
Virchow, R.: Die Krankhaften Geschwülste, Berlin **1**: 69, 1863.

Note.—A recent tabulation of the sites of metastases in a series of patients who died with cervical carcinoma included another instance of metastasis of the breast. (De Alvarez, R. R.: Am. J. Obst. & Gynec. **54**: 91, 1947.)

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Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

Review of New Books

Gynecology and Obstetrics

Dr. Trussell presents in this report, **Trichomonas Vaginalis and Trichomoniasis,**[1] the present status of our knowledge of trichomonas vaginalis. A tremendous amount of literature has been developed since this organism was first suggested as an etiologic factor in vaginitis by Hoehne in 1916, and Dr. Trussell has rendered a fine service in evaluating this material. More particularly, he has interested himself in the life history of the parasite, its growth requirements in attempting to produce a pure culture, its biochemical activities, and the effect of various physical and chemical agents on its viability and pathogenicity. He discusses not only the *T. vaginalis* but also the other parasites of a somewhat similar nature.

The second part of the book is an extended discussion of the infections caused by the parasite as to the location, source, recognition, prognosis, and clinical findings. Dr. Trussell does not feel from his own investigations that women harboring *T. vaginalis* have an increased tendency to a morbid puerperium.

Treatment, the author states, since 1916, has been a series of "trial and error" experiments. Much of the treatment, he says, has been based on a combined effort to eliminate not only the *T. vaginalis,* but also the associated abnormal microflora. Dr. Trussell feels that the two most effective methods of vaginal medication are powder insufflation and jellies, the latter adjusted to an acidity favoring normal vaginal biology. He states that as yet no specific therapeutic agent has been discovered and the various drugs and chemicals used in recent years are listed in some 59 pages. This multiplicity reflects the general lack of success obtained.

The book closes with a discussion of the taxonomic relationship of trichomonas to other protozoa, a parasite-host list of trichomonads, as well as a bibliography.

Studies of this type on the biology, growth requirements, and various relationships of the parasite should, one feels, soon lead to the discovery of a specific agent for the eradication of such infection which, while not as severe as similar infections in animals, still has a high nuisance value to both the patient and the clinician.

PHILIP F. WILLIAMS.

Dr. McCormick's fine monograph on **Pathology of Labor, the Puerperium, and the Newborn**[2] appears in its second edition with an increase of one hundred pages to include the advances and new techniques, while almost the same number of new illustrations have been added to correlate the added material. Among the major revisions is a discussion of the Caldwell-Moloy classifications of the female pelves. While acknowledging the tremen-

[1] **Trichomonas Vaginalis and Trichomoniasis.** By Ray E. Trussell, M.D., Associate in Hygiene and Preventive Medicine, Former Research Assistant in Obstetrics and Gynecology, State University of Iowa, with an Introduction by E. D. Plass, M.D., Professor of Obstetrics and Gynecology, State University of Iowa, Charles C Thomas, Springfield, Ill., 1947

[2] **A Textbook Pathology of Labor, the Puerperium and the Newborn.** By Charles O. McCormick, A.B., M.D., F.A.C.S., Clinical Professor of Obstetrics, Indiana University School of Medicine, Consulting Obstetrician to William H. Coleman Hospital for Women, Indianapolis City Hospital, and Sunnyside Sanitarium, Second Edition, 492 pages, with 272 illustrations, including 24 in color, The C. V. Mosby Company, St. Louis, 1947.

dous help of pelvioradiography, Dr. McCormick feels that such studies must always remain secondary to clinical examination and judgment. The Burns maneuver for the delivery of the aftercoming head, which does not employ shoulder traction, and which avoids jaw flexion, is described and illustrated. It has been successful in the hands of the author.

Dr. McCormick, who is a firm believer in prophylactic external version in breech presentations, has rewritten this section, particularly with regard to technique. For impaction of the shoulder he describes a technique which has been found eminently successful in his clinic in recent years. This corkscrew maneuver undoubtedly would be useful in the occasional emergency of this nature. There is an excellent review, with concise directions as to treatment, of the anticoagulants in the prevention and treatment of deep thrombophlebitis.

The conflicting opinions as to the handling of the diabetic in labor are discussed in an expanded section on this topic. McCormick prefers vaginal delivery when possible. He stresses the availability for prompt treatment of shock and other situations which bring about sudden death during labor. In the excellent section of the book devoted to pathology of the newborn, the text regarding the Rh factor and hemolytic disease in its various manifestations is augmented. The author has pointedly advised checking the Rh situation in all obstetric transfusions.

An appendix carries a very thorough discussion of different types of pain relief in labor. The author concludes with the statement that analgesia and anesthesia must remain secondary to maternal and fetal welfare. The appendix also describes a series of puerperal exercises. In regard to the early ambulation of puerperal patients the author anticipates an increased amount of retroversion and prolapse of the uterus, and associated disturbances from this practice. From a psychological aspect he feels that a puerperal patient is not only entitled to, but profits by, extra days of hospital rest. The obstetric aspects of the Canon laws of the Roman Church are well included. Once again the reviewer is favorably impressed with the complete coverage of the three subjects in the title and the clarity and conciseness with which they are set forth.

PHILIP F. WILLIAMS.

In this excellent **Synopsis of Obstetrics**,[3] now in its third edition, the author has added advances and rewritten five different subjects, yet by adhering to the original idea of a brief although adequate discussion, the book gained only twenty pages over the first edition. There is new material on the biologic hormone tests of pregnancy. An excellent review discusses the presently suggested methods of relieving pain in labor, and it is well that space has been given to the dangers, difficulties, and contraindications of the methods mentioned. Litzenberg has stressed the difficulties encountered with every type of pain control, in order that caution instead of enthusiasm will characterize our acceptance of every new proposed method.

The importance of good diabetic care, in the successful handling of pregnancy in such cases, is emphasized, and he describes the substitutional hormone therapy to prevent toxemia and to promote fetal survival, which, while slowly gaining acceptance, seems still a moot point. The more specific bacterial indications for penicillin or the sulfa drugs in obstetric complications are stated. The prophylactic use of either agent with premature rupture of the membranes or presumably infected labor is, however, not mentioned.

In the discussion of the Rh blood factor in pregnancy, Dr. R. W. Koucky has furnished a very clear and concise résumé of this important problem. In answer to the question, "What type blood should be given to the erythroblastotic baby?" he feels that Rh-negative blood only maintains hemoglobin, whereas a transfusion of Rh-positive blood may divert some of the antibody from the baby's tissues, a desirable conservation.

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[3]**Synopsis of Obstetrics.** By Jennings C. Litzenberg, B.Sc., M.D., F.A.C.S., Professor Emeritus of Obstetrics and Gynecology, University of Minnesota Medical School, Minneapolis, Third Edition, 399 pages with 157 illustrations including 5 in color, The C. V. Mosby Company, St. Louis, 1947.

The incorrect legend for Fig. 140 is still present, as in the first edition. No doubt there will always be a place in any division of medicine for a synopsis as well prepared and as well worth while as this one is for obstetrics.

PHILIP F. WILLIAMS.

In this book, **Rh, Its Relation to Congenital Hemolytic Disease and to Intragroup Transfusion Reactions,**[4] Dr. Edith L. Potter, whose unusual experience in the pathology of the fetus and newborn, and fortunate connection with an outstanding maternity hospital have eminently fitted her for the task, has reviewed the extensive literature of the subject and brought it thoroughly digested and logically arranged for our understanding of a very complicated subject.

Dr. Potter opens the discussion with a general survey of the whole problem. Briefly she reviews the discovery of the Rh antibody in rabbits, in recently pregnant women, and the relation of the antibody to transfusion reactions. The survey continues through the characteristics, varieties, inheritances, and racial differences of Rh. The mechanism of immunization is followed by the relation of the Rh to transfusion reactions and to congenital hemolytic disease. The basic principles of determination of Rh character of blood and detection of Rh antibodies are explained.

The importance of the Rh status of the blood to the welfare of a pregnant woman and her infant, both before and after birth, and to anyone who needs a transfusion is emphasized. While one realizes that the continuing literature on the subject keeps the topic in a state of flux, one can also feel that this digest and correlation has missed nothing of note in the material presented to date.

In ensuing chapters Dr. Potter expands on the topics discussed in the general survey. The background of blood grouping, the mechanism of antibodies, the production of immunization and the development of our present blood type system are presented. The theories and studies of intragroup reactions and incompatibility, particularly in the obstetric field, as to toxemia and fetal death, are discussed, together with the research on blood group incompatibilities. Dr. Potter describes the discovery of the Rh factor and the review of transfusion reactions and stillbirths in recent pregnancies from which the evidence of maternal isoimmunization became apparent.

The story of Rh antigens and antibodies is continued as to the physical properties and specific characteristics and the mode of immunization in pregnancy. An interesting paragraph discusses Darrow's postulating correctly the antigenic difference which makes possible maternal sensitization to the fetus, three years before the Rh antibody, a specific antigen, was discovered.

Further in this chapter, Dr. Potter portrays the enlargement of the Rh blood types, illustrated by expanding classifications Wiener offered in 1943, 1944, and 1945, and she clearly explains the complexities of the subtypes which have arisen as further investigative work has proceeded. The inheritance of Rh and Hr by the postulated presence of eight alleles is described and illustrated. The use of various anti-Rh and anti-Hr sera in establishing the possibility of paternity is set forth. In discussing the nomenclature of Rh and Hr, Dr. Potter feels that the plan proposed by Fisher is convenient and equally sound for whatever form of inheritance is finally found to be correct. Certainly a simple uniform nomenclature would help greatly in understanding the publications on the subject. In discussing racial incidence of Rh, she states that where race-crossing is negligible the blood groups probably remain constant for long periods. There is a very clear presentation of the relation of Rh and transfusion reactions. Many practical suggestions are made in this section.

There is an extended discussion of the subject of hemolytic disease, historically, when the cause was unknown and the three varieties appeared to be distinctly different entities, together with the many hypotheses offered in those days, as well as our present understanding

[4] **Rh, Its Relation to Congenital Hemolytic Disease and to Intragroup Transfusion Reactions.** By Edith L. Potter, M.D., Ph.D., Assistant Professor of Pathology, Department of Obstetrics and Gynecology, The University of Chicago and the Chicago Lying-in Hospital, 336 pages with 65 illustrations, The Year Book Publishers, Inc., Chicago, 1947.

of the disease with its clear etiological basis. The reason for the rarity of the disease in the first pregnancy is discussed from the standpoint of four main possibilities.

The various clinical contradictions reported, such as hemolytic disease in Rh-negative infants, are discussed and explained. The pathology and clinical course of the disease, diagnosis, complications, and treatment are amply discussed. Dr. Potter does not feel that exsanguination transfusions provide a sufficiently improved outlook for the life of the child to warrant encouraging their use. Postmortem studies and the pathology of the various types of hemolytic disease are thoroughly described.

The final chapter of the book provides discussions for a simple determination of the Rh status of blood cells and the presence of antibodies, as well as the more elaborate technical procedures necessary in differentiating the present varieties of antibodies and antigens. The bibliography lists 794 references to the literature which have been reviewed in the text.

The book is an outstanding résumé and discussion of this all-important subject. The book not only condenses and presents the important papers, but gives as well the experience and knowledge of an interested worker in the field. The book should be of great value to obstetricians, pediatricians, and clinical pathologists, and is highly recommended.

PHILIP F. WILLIAMS.

This small, but thoroughly complete and well-documented volume, **The Premature Baby,**[5] sums up the fourteen-year-long experience of Dr. Mary Crosse in this particularly important field of medicine in the hospitals and homes of Birmingham, England.

The exigency of the problem lies in the fact that one-half of all deaths of babies in the first month of life are due to their being born prematurely. The description of methods for salvaging prematurely born infants is full and complete; the author is meticulous in describing small but essential details. Together with her own procedures, she adds and describes the successful practices of other workers in the field. The need for well-equipped and staffed premature stations is stressed, and care of prematures from such angles as transport, types of incubators, and prevention of infection is given.

The discussion on the care of the premature under less auspicious circumstances, the home, is full of practical simple suggestions. There is an extensive consideration of feeding, complications, and infection. Over a period of thirteen years Dr. Crosse has achieved the gratifying neonatal mortality rate of but 128 deaths per 1,000 premature live births.

As to the causes of prematurity, in which the readers of this JOURNAL may be more interested, Dr. Crosse rates toxemia of pregnancy, 29 per cent, and multiple pregnancy, 10 per cent, as the most frequent. Unknown etiology was responsible for 38.5 per cent. In two-thirds of this latter group, a history was obtained of two or more previous premature labors or miscarriages. This excellent volume is replete with valuable information for the pediatrician, obstetrician and, premature-station staff.

PHILIP F. WILLIAMS.

Miscellaneous

The importance of cancer as a factor in human mortality makes the appearance of a practical text, such as this volume, **Cancer, Diagnosis, Treatment, and Prognosis,**[6] by Ackerman and Regato, very timely.

The first five chapters of the book are devoted to subjects of general interest in the whole field of malignant neoplasm. Dr. Michael B. Shimkin, of the staff of the National

[5] **The Premature Baby.** By V. Mary Crosse, M.D. (London). D.P.H., M.M.S.A., D.R.G.O.G., Chief Obstetric Officer in charge of City of Birmingham Maternity Homes and Premature Baby Unit; with Foreword by Leonard G. Parsons, M.D., F.R.C.I., F.R.C.O.G., Professor of Children's Diseases, University of Birmingham; 142 pages with 14 Illustrations; The Blakiston Company Philadelphia, 1947.

[6] **Cancer, Diagnosis, Treatment, and Prognosis.** By Lauren V. Ackerman, M.D., Pathologist to the Ellis Fischel State Cancer Hospital; Assistant Professor of Pathology, Washington University School of Medicine, St. Louis, and Juan A. del Regato, M.D., Radiotherapist to the Ellis Fischel State Cancer Hospital; Formerly Assistant to the Radium Institute of the University of Paris; 1075 pages, with 745 text illustrations and 42 color reproductions, The C. V. Mosby Company, St. Louis, 1947.

Cancer Institute, has written an extended and illuminating story of cancer research in which he discusses the role of heredity and the other etiological factors, the characteristics of cancer, the transplantation of tumors and the development of present-day therapies. In discussing the influence of estrogens and other hormones, Shimkin concludes that estrogenic compounds may initiate in some unknown way a number of neoplastic processes, usually of tissues that are normally under the influence of sex hormones.

In the chapter on pathology of cancer, there is a thorough description of the collection and preparation of specimens and the microscopic distinctions, as well as a discussion of the nature of the various growths, their characteristics and methods of extension.

Dr. Bricker, who has edited the chapter on surgery, importantly stresses the need for extensive surgery in extirpating malignant lesions, and concisely discusses the pre- and postoperative care, the selection of anesthesia, and the neurosurgical procedures for relief of pain in advanced cancer. The physical foundation of radio-therapy, the measurement of its quantity and quality, and its biologic effects are discussed generally, followed by practical facts on the clinical use, technical aspects, and limitation of its use as a therapeutic measure.

The remainder of the text is divided according to systems and the particular type of tumor and tissue involved. The discussion of these topics follows the same outline, from anatomy through to prognosis, giving a definite completeness to each presentation.

Malignant conditions of the female pelvic organs form one-sixth of the book. Ovarian tumors are classified, both as to their origin and type, but discussed according to the latter. This section of the book is profusely illustrated with many color plates. The rare types of ovarian tumors are particularly discussed in regard to their ancestry and diagnosis. How extensive an operation is necessary in finding a unilateral ovarian tumor is relatively answered by the authors in an interesting table on the indications for surgical treatment of ovarian tumors.

The important recent literature on carcinoma of the endometrium is amply brought into the discussion of this topic. The authors contrast the American method of hysterectomy when practicable, the use of preoperative radium therapy, and the use of radium in inoperable cases, with Heyman's dissenting opinion that radium alone is the treatment of choice. Considerable space is devoted to the clinical classification of the carcinoma of the cervix. The authors present a series of general rules to aid an examiner in making clinical classifications for fair comparison. Several pages of illustrations are included to bring out the points necessary in making a clinical classification.

Discussing diagnosis, the authors feel that the vaginal smear method cannot compete with the standard methods, such as biopsy of the cervix and dilatation and curettage of the endocervix. In a prophylactic survey of nonsymptomatic women in which biopsy and curettage would not be justified, the examination of vaginal smears may contribute (although at the expense of valuable time and effort) a few early diagnoses of cancer of the uterus.

The evolution of treatment of cancer of the cervix is discussed and the currently used techniques of various clinics are detailed. The authors state, "We believe that thorough external radiation of the pelvis is an important first step in the treatment of all cases of cervical cancer," and again, "If internal radiation can be called the most important single factor in the treatment of early cases, thorough external roentgen therapy is the most important single factor in the treatment of advanced cases." The question of total hysterectomy in nonmalignant lesions is logically regarded by the authors as a question of balance between the greater operative mortality of the radical operation and the incidence of carcinoma in the remaining cervix. There is an excellent discussion of the carcinoma of the cervix in pregnancy and of malignancy of the lower genital tract.

Following the presentation of mammary carcinoma and other remaining systems, the authors give an excellent review of the present opinions on research in, and treatment of, Hodgkin's disease and leucemia.

The excellence and completeness of the presentation and the balance achieved by the dual authorship of a pathologist and a radiotherapeutist make the text an outstanding contribution on this subject.

PHILIP F. WILLIAMS.

The **Acute Infectious Fevers,**[7] an introduction for students and practitioners by Dr. Alexander Joe, is divided into fifteen chapters. One concludes, after perusing the book, that the endeavor of the author to answer fundamental questions which are repeatedly asked by students and house officers on the subject has been eminently successful.

The author feels that the result of Dick tests show that women in the puerperium are not more susceptible to scarlet fever than others in the same age group. He does not feel that scarlet fever in childhood predisposes to renal lesions in maturity. The author notes a sensible diminution in the mortality from sepsis in the British Isles, which he attributes to the widespread use of the sulfonamides; he feels an increasing proportion of the sepsis deaths there are due to postabortive sepsis. He recommends the immediate prophylactic use of these drugs after a traumatic labor. The intrauterine instillation of glycerine in sepsis, which he describes, is not a part of the therapy in this country.

The safeguarding of pregnant women, especially during the early months, from contact with rubella cases is emphasized, although no definite statement is offered as to occurrence of congenital defects in the offspring of such affected mothers.

PHILIP F. WILLIAMS.

In the second edition of **Communicable Diseases,**[8] by Dr. Top and his collaborators, fourteen new chapters have been added. The book is intended as a text and handy reference for all persons whose professional contacts necessitate connection with certain communicable diseases. An excellent chapter in the section of general consideration on the management of communicable diseases in hospitals leaves little to be desired in regard to the care of the patient, not only from the administrative standpoint, but also as to nursing, laboratory procedures, and prevention of cross-infections.

The author has classified communicable and infectious diseases by a common portal of entry, and, further, by the etiological factors as fungi, bacteria, or viruses. Considerable space is devoted to the specific prevention of certain communicable diseases, and there is a chapter on serum and serum reactions.

In discussing German measles and the congenital defects in infants attributed to such infection in early pregnancy of the mother, Top feels it is still too early to assess fully the complications of the reported findings. He feels that the study has been approached from the wrong end, namely, the affected child. He proposes that the pregnant women should be studied in two groups, those who did and those who did not contract German measles during pregnancy, and then the abnormalities in the children of both groups should be noted; differences then might be considered significant. He suggests the use of human immune globulin in the treatment of German measles in early pregnancy, but feels that therapeutic abortion should not be indicated.

In discussing epidemic diarrhea of the newborn, Cummings feels that a filtrable virus is the infectious agent. He discusses the epidemiology of the disease, refers to the lack of significant pathology and to the lack of immunity. He notes that epidemics are more severe when the premature population of a nursery is high, stresses the difficulty of dif-

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[7]**The Acute Infectious Fevers, an Introduction for Students and Practitioners.** By Alexander Joe, D.S.C., M.D. (Ed.), F.R.C.P. (Ed.), D.P.H., D.T.M. & H., Medical Superintendent, City Hospital, Edinburgh. Lecturer on Infectious Diseases to the University of Edinburgh. Formerly Medical Superintendent, North-Western Hospital, London. 266 pages with 64 Illustrations. The Blakiston Company, Philadelphia, 1947.

[8]**Communicable Diseases.** By Franklin H. Top, A.B., M.D., M.P.H., F.A.C.P. Medical Director, Herman Kiefer Hospital; Clinical Professor of Preventive Medicine and Public Health, Wayne University College of Medicine; Consultant, Preventive Medicine Section, Surgeon General's Office, United States Army, and Collaborators. 948 pages with 95 illustrations and 13 Color Plates, Second Edition, The C. V. Mosby Company, St. Louis, 1947.

ferential diagnosis, and gives an excellent practical schedule for treatment, recommending sulfadiazine. His suggestions for preventability and control state, concisely, a rigid nursery technique.

In discussing chancroid, Shaffer states that the sulfonamides have revolutionized the treatment of chancroid, and refers to the 20 per cent sulfathiazole content of the new Army prophylactic. The same contributor, in an excellent discussion of lymphogranuloma venereum, states that the sulfonamides are the most practical method of treatment now available, that the Frei antigen is much less effective. Penicillin, he says, seems to have no effect in this disease.

Granuloma inguinale, according to Shaffer, is uncommon in Detroit, not over twenty cases annually presenting themselves in the Social Hygiene Clinic. He refers to the difficulty in diagnosis, as the type of person affected has often had such previous infections such as syphilis, lymphogranuloma venereum, and chancroid. Antimony is regarded as the most effective therapy, while penicillin and the sulfonamide group have not been found of value.

Each chapter gives its own bibliography, while an appendix analyzes the communicable diseases seen in the Herman Kiefer Hospital in Detroit over a long period of years. The text is comprehensive from both a curative and a preventive standpoint of the disease discussed, and should be found helpful in many types of practice.

PHILIP F. WILLIAMS.

The lectures to the laity in the March of Medicine Series of the New York Academy of Medicine for 1945 are devoted to **Modern Attitudes in Psychiatry.**[9] There are six lectures, each by an outstanding authority in the field, which logically and effectively portray the history and development of this branch of medicine, its application to the individual patients, its possible future trends, its usefulness during the recent war, and its application to the recurrent problems of daily practice. To those who may not have realized the important relations of social and environmental problems of the individual patient to his illness, this book is warmly commended.

PHILIP F. WILLIAMS.

[9]**Modern Attitudes in Psychiatry.** The March of Medicine, 1945, 150 pages, Columbia University Press, New York, 1946.

Department of Reviews and Abstracts

Selected Abstracts

Endometriosis

Ahumada, J. C., and Nogues, A. E.: Perforating Fornix Endometriosis, Obst. y Ginec. Latino-Am. **4**: 651-666, 1946.

The authors have observed 232 women with endometriosis. Among these 12 or 3.4 per cent had endometriosis of the recto-vaginal septum with perforation through the vagina. Brief histories are given of these twelve cases. The symptoms characteristic of perforation of endometriosis of the recto-vaginal septum are as follows: metrorrhagia, premenstrual and intramenstrual pain sometimes associated with rectal pain, and infiltration of the vagina by the tumor resulting in folds and wrinkles in the vagina. Often hemorrhagic cysts are observed and a later development are soft polypoid structures presenting a dark, bluish red tint.

There are three pathologic types: (1) the primary type, (2) the type which is secondary to continuous growth from the adnexa and (3) the type which results from endometriosis of the uterus.

The treatment of choice is surgical, being conservative in women under 40 and radical after this age. If there is a contraindication to surgery, roentgen therapy should be used. Radium is not beneficial. The prognosis is good. All the patients in this series were cured.

J. P. GREENHILL.

Gynecology

Alfieri, P.: Angioma of the Vulva, Clin. ostet. **48**: 145, 1946.

Angioma of the vulva is an uncommon finding. Alfieri thoroughly reviews the literature on the subject and describes a case of cavernous angioma of the vulva in which both labius majus and the clitoris were involved, a quite unique localization previously noted only by Taussig.

The tumor was present at birth, however, had been growing progressively since, and its histologic features readily differentiate it from a congenital anomaly (amathoma) so often classified as, and confused with, blood vascular tumors.

The angioma appeared mainly composed of large venous cavities lined with vascular endothelium, containing blood in large quantities. A negligible amount of fibrous stroma was present. At the periphery, the growth appeared made up of capillaries with a minimal amount of supporting stroma. No other tissue was present, nor was more significant parvicellular infiltration seen.

The patient was cured by surgical ablation of the tumor. GEMMA BARZILAI.

De Giorgi, L.: Sudoriferous Gland Tumor on the Labia, Arch. di ostet. e ginec. **51**: 119, 1946.

De Giorgi reviews the continental literature on the subject and describes a case of sudoriferous gland adenoma of the labia. The tumor was boggy on palpation and micropictures presented, as well as the microscopic description, correspond to features of what in this country is called hydradenoma papilliferum. The growth was well encapsulated and made up of cystic and papillary portions. The epithelium appeared arranged in two layers, one corresponding to the secretory lining of sudoriferous glands, the other to the outer myoepithelial layer.

GEMMA BARZILAI.

Calmenson, Marvin, Dockerty, Malcolm B., and Bianco, John J.: Certain Pelvic Tumors Associated With Ascites and Hydrothorax, Surg., Gynec. & Obst. **84**: 181, 1947.

Nine instances of a pelvic tumor associated with ascites were found in approximately 20,000 records of pelvic tumors. These cases are reported in detail. The ovarian tumors were all large, averaging 16 cm. in diameter and included five ovarian fibromas, one degenerating uterine fibromyoma, one fibromyoma of the uterus with pelvic inflammatory disease, one granulosa cell tumor and one teratoma of the ovary. The major contribution of the paper is the suggestion that the development of the ascites is related to the edema and large size of these tumors. To substantiate this it was noted that fify-one tumors which were accompanied by ascites showed edema in 96 per cent while only 10 per cent of tumors unaccompanied by ascites showed edema. The theory for development of hydrothorax is discussed but no conclusive proof as to the origin of this fluid is offered.

M. HELLMAN.

Gynecologic Operations

da Silva Loureiro, O.: Vaginal Hysterectomy for Nonmalignant Conditions of the Uterus, An. brasil de ginec. **22**: 276-281, 1946.

At the Gynecologic clinic of the Brazil National Faculty of Medicine, 57 vaginal hysterectomies were performed for nonmalignant conditions of the uterus. The principal indications were prolapse of the uterus with cervical erosion, 30; interstitial fibromyoma of the uterus, 13; and glandular hyperplasia of the uterus with metrorrhagia, 9. There were no deaths in this series. The ages of the patients varied from 41 to 74 years. The Mayo-Kelly operation was used in the prolapse cases, and the Martius technique was employed in the other cases. Local anesthesia was used in all of the cases.

J. P. GREENHILL.

de Aquino Salles, A., and Conri, A. A.: Bilateral, Simultaneous Uretero-Entero Anastomosis According to the Davalos Technic in the Treatment of Incurable Vesicovaginal Fistulas, An. brasil de ginec. **22**: 263-275, 1946.

The authors report two cases of incurable vesicovaginal fistula treated by bilateral simultaneous ureterointestinal implantation according to the Davalos technique. These may be the first cases in which the operation was performed on human beings. The operation is simple and does not interfere with the flow of urine. The use of sulfonasuxidine helped considerably. Transient anuria was present until the third day but subsided spontaneously. Intravenous urographic studies showed that hydroureters developed after operation but that progressive improvement followed this occurrence.

J. P. GREENHILL.

Labor

Hansen, Jens L.: Spinal Anesthesia as Therapy in Cases of Postpartum Uterine Atony, Acta obst. et gynec. Scandinav. 22: 1943.

Hansen proposes the use of low spinal anesthesia in cases of postpartum hemorrhage caused by uterine relaxation, based on his experience with four cases. He feels that a spinal should be given after "the usual extragenital measures" (oxytocic and uterine massage) have failed. The reaction of the individual reader to the author's suggestion that spinal anesthesia be used before such comparatively simple measures as uterine packing are tried is unimportant as compared to the clarity with which Hansen emphasizes the fact that any postpartum bleeding in excess of 500 c.c. is serious and calls for immediate action. He urges that every accoucheur must have planned beforehand just how he will cope with every case of postpartum hemorrhage. He must know how much time will be allowed to elapse and how much blood lost before a more active step is taken. Naturally, blood transfusion is the most important of all these steps.

HERBERT J. SIMON.

Tonkes, E.: Rupture of the Membranes Before the Onset of Labor, Gynaecologia **123:** 58-72, 1947.

Tonkes, of Middelburg, Holland, reviews the infant mortality of his country and compares it to other continental countries as an introduction to his article. These figures are significant. During the years 1924 to 1939, there were 2,675,018 deliveries in Holland with 68,137 stillbirths; an incidence of 2.547 per cent. This percentage was compared to The Hague statistics for the near period of 1929 to 1936, and revealed the stillborn percentage for Germany was 2.83; Belgium, 3.24; England, 4.07; Australia, 2.77; France, 3.35; and Switzerland, 2.26 per cent.

In the effort to improve the fine Dutch figure, the author considers the role of premature rupture of the membranes and its possible relationship to stillbirths. In his opinion, this procedure is dangerous, and is the cause of increase in infant mortality. To support his impressions Tonkes collected sixty-six cases. In this group occurred two maternal deaths, seventeen stillbirths, three cases of neonatal cerebral hemorrhage and one case of imbecility. He emphasizes that to overcome uterine atony often seen with premature rupture of the bag of waters pituitrin is indicated in mothers with normal pelves to accelerate labor prior to the end of the second stage. In cases with borderline bony parts vaginal cesarean section is indicated, according to Tonkes.

C. E. FOLSOME.

Amorin, J., Lacreta, O., and Endrizzi, L.: Pregnancy and Labor in the Presence of Excessively Large Babies, An. brasil de ginec. 22: 393-401, 1946.

The authors reviewed the records of 3,173 pregnant women and found that 120 had given birth to babies which weighed more than 4 kg. (8.8 pounds). This is an incidence of 3.7 per cent. More than one-half of the mothers of the 120 babies were between 25 and 35 years of age, and the following complications were associated with the gestation: malaria, 12 per cent; syphilis, 5 per cent; heart disease, 0.83 per cent; and hyperthyroidism, 0.83 per cent. Hypertension was present in 20 per cent, and in 19 per cent the pregnancy went beyond three hundred days. The membranes ruptured spontaneously in 76 per cent of the cases. Dilatation of the cervix required more than twelve hours in 41 per cent. Labor was normal in 82.5 per cent. Operative deliveries were as follows: forceps, 8.53 per cent; cesarean section, 0.83 per cent; Zarate symphysiotomy, 0.83 per cent; external version, 0.83 per cent; and embryotomy, 1.66 per cent. Among the mothers there was one case of shock, perineal laceration in 7.5 per cent, and vaginal cervical lacerations in 3.33 per cent.

In 10 per cent of the cases bleeding was excessive. Fetal asphyxia occurred in 10.83 per cent. and the incidence of fetal death was 4.16 per cent. The puerperium was normal in 75 per cent. J. P. GREENHILL.

Heffernan, Roy J., and Sullivan, Charles Leavitt: Complete Absence of Lochia Following Delivery. New England J. Med. 236: 65, 1947.

The case of a 40-year-old primigravida delivered by cesarean section four weeks before term is presented by the authors. Vulva pads were carefully inspected, and remained perfectly dry during her entire convalescence. On the twenty-first day following delivery, menstrual flow began.

Two possible explanations are given. JAMES P. MARR.

Barnes, Josephine: Pethidine in Labor: Results in 500 Cases, Brit. M. J. 4500: 437-442, 1947.

Pethidine is an English proprietary name for 1-methyl-4-phenyl-peperidine-4-carboxylic acid ethyl ester hydrochloride. It is known as ''dolantal'' in Germany, as ''dolantin'' in South America and as ''demerol'' in the U. S. A. and Canada, where it was also termed S-140 and D-140. Actually the drug was introduced as a synthetic substitute for atropine.

Barnes reviewed the results following use of pethidine in labor among 500 patients, 479 primigravidas and 21 multiparas on the Obstetric Unit of the University College Hospital. There was no maternal mortality. Eleven mothers noted slight toxic symptoms—characterized by dizziness, or feeling of faintness, giddiness or numbness, sweating, and slight retching. The effects were said to be transient.

The fetal mortality was sixteen stillbirths, 3.2 per cent, and five neonatal deaths, 1.0 per cent. Signs of asphyxia were noted in fifty-five infants, 11.0 per cent; recovery occurred in all. Pethidine may have contributed to slight respiratory depression in a few cases.

Good analgesia was experienced by 55.0 per cent of mothers. Perhaps in some failure the drug may have been given too late. Amnesia was obtained in only 10.0 per cent. Some symptomatic relief was experienced by 87.0 per cent of the cases. No effect on uterine contractions was noted in 67.0 per cent. In 23.3 per cent contractions appeared to increase, while in 8.7 per cent they seemed to decrease.

The duration of labor was compared in primigravidas with a control series of patients delivered in 1939. It was found that the first stage was seven hours longer in patients receiving pethidine (''demerol''). The claim that pethidine shortened labor could not be substantiated.

The forceps rate was 9.2 per cent, as compared to 7.8 per cent in the control series of 1939. No tendency to postpartum hemorrhage was observed. Pethidine was given as premedication for cesarean section in 32 cases. Although this drug did not fulfill all the Sturrock criteria as an ideal analgesia, it seemed to approach this ideal more nearly than any other obstetric analgesic in current use. C. E. FOLSOME.

Miscellaneous

Hattersley, Lt. Paul G.: Two Popular Fallacies Regarding Rh, J. Lab. & Clin. Med. 32: 423, 1947.

The author presents data to correct two fallacious Rh beliefs which he fears are widespread:

(a) The belief that sensitization of Rh-negative persons by Rh-positive blood transfusion is infrequent; in his group blocking Rh antibodies were demonstrated in 55 per cent by the use of albumin-suspended cells.

(b) The belief that blocking antibodies are always of Rh_0 specificity; by the use of the albumin-suspended cell technique he demonstrated Rh′ antibodies in 60 per cent and RH″ antibodies in 15 per cent of his apparently nonreacting (saline-suspension) sensitized group.

This work emphasizes the importance of properly prepared sera. S. B. GUSBERG.

Perez, M. L., and Echevarria, R.: Prophylactic Intraperitoneal Sulfonamide Therapy in Obstetric Surgery and in Impure Cases, Obst. y Ginec. Latino-Am. 4: 447-552, 1946.

The authors reviewed the literature and studied their own obstetric cases where the sulfonamides were used as a prophylactic measure. In a series of more than 700 cases, the mortality in the group which received sulfonamides prophylactically was 0.81 per cent as contrasted with a death rate of 4.3 per cent for the group which were not given the sulfonamides. Among the 613 patients who had had transperitoneal cesarean sections and were given the sulfonamides prophylactically, the maternal mortality was 0.32 per cent. This is considerably below the incidence of 3.33 per cent which is the mortality rate usually quoted for extraperitoneal cesarean sections.

The authors' choice of cesarean section is the Opitz transperitoneal type. There were no deaths from peritonitis. In their last twenty-eight cases of unclean cases the authors added penicillin therapy to the intraperitoneal sulfonamide treatment and the results were so strikingly good that they believe the problem of cesarean section in impure cases has been solved. J. P. GREENHILL.

Puerperium

Wassenaar, J. J. S.: Postpartum Intra-abdominal Separation of Uterus, Brit. M. J. 4500: 452, 1947.

The patient, a 25-year-old primipara, purportedly gave birth to a male infant, in her home, after a labor of eight and one-half hours. The attending nurse could not expel the placenta by simple means. A physician was called. He administered two doses of ergometrine and one dose of calcium gluconate. Seven hours after delivery the patient was admitted, in shock, to the Germiston Hospital. After control of shock, a twenty-five-minute attempt to manually remove the placenta revealed omentum. The author was called and, concurrent with more anti-shock treatment, a laparotomy was done.

The uterus was found completely severed, and only three relatively small bleeding points seen. The stretched cervix was torn through and severed from the body of the uterus; the Fallopian tubes were torn off separately; the ovaries were intact. There was no damage to ureters or adjacent visceral organs. The uterine arteries could not be found. The patient, with use of postoperative sulfadiazine and penicillin, left the hospital on the seventeenth day. Examination of the specimen revealed long pieces of uterine arteries attached to the specimen, apparently torn off at their origins from the internal iliac arteries.

The author concludes by asking numerous questions without attempting to answer them, for whatever the answer, this case, in his opinion, was without parallel in view of the severity of the lesion and the survival of the patient. C. E. FOLSOME.

Barnes, Allen C.: Postpartum Blood: Its Clotting Mechanism and Relationship to the Peripheral Blood Picture, Am. J. M. Sc. 213: 463-469, 1947.

Barnes, Ohio State University Medical School, restudied the "coagulation defect" of postpartum uterine blood. This blood fraction does not clot in vitro spontaneously or on the addition of the following substances singly: calcium, thromboplastin, trypsin, fibrinogen or thrombin. Therefore, it does not resemble oxalated, citrated or heparinized bloods, or recalcified plasma. Postpartum blood will clot upon the addition in excess of a mixture of thrombo-

plastin and fibrinogen, or on "seeding" with small amounts of freshly drawn venous blood. It displays a clot promoting action and a definite, but weak, proteolytic activity. Thus it behaves in a manner similar to defribinated blood or a suspension of cells in serum.

The hematologic and chemical characteristics of postpartum uterine blood were investigated. Its cell count varied daily during the puerperium. This variation gave a characteristic pattern, with a steady fall in the hemoglobin and red cell count and a rapid use in the white cell elements.

Variations in the clotting mechanism of the peripheral blood on the amount of postpartum blood loss were measured. Prolongation of the prothrombin and clotting times (by dicumarol and heparin) did not decrease the amount of postpartum blood lost. The administration of vitamin K was without effect in raising the (already elevated) prothrombin level of the patient immediately postpartum, and was without effect in diminishing vaginal blood loss.

Barnes states that the most important single factor influencing the amount of blood loss following delivery is the mechanical closing of the sinuses in the placental bed, which is dependent upon the efficiency of the uterine contraction and unrelated to the coagulation tendencies in the circulating blood. Therefore, no definite relationship could be established between the peripheral blood coagulability and the amount of postpartum bleeding.

C. E. FOLSOME.

Toxemia

Krieger, Vera I., and Weiden, Sara: The Value of the Cold Pressor Test in the Prediction of Hypertension and Toxemia in Pregnancy, M. J. Australia 1: 417-423, 1947.

The authors, of the Department of Pathology, Women's Hospital, Melbourne, re-evaluate the cold pressor test of Hines and Brown. In a series of 522 cold pressor tests performed during 200 pregnancies, all tests gave normal results in eighty-four instances, hyperaction to the cold stimulus occurred in one test only on each of thirty-one patients and in more than one test on each of eighty-five patients. Only thirteen of the patients, all of whose cold pressor tests gave normal results, developed hypertension in the latter part of their pregnancies. Four of this group developed pre-eclampsia.

In a group of 506 patients in which no cold pressor tests were made during pregnancy, basal blood pressure readings and cold pressor tests were made two months after the completion of pregnancy. In 12 per cent of these normal cases there was an abnormal response, but this figure increased to 36 per cent when the patients had had mild toxemia. After pre-eclampsia more than 50 per cent gave hypertensive evidence.

The writers concluded the results of the cold pressor tests during pregnancy were of value to the obstetrician, since, even if only one response in the series was of the hyperactive type, 50 per cent of the cases giving such responses developed hypertensive or preclamptic toxemia. When two or more abnormal results were obtained, the number of patients who developed toxemia increased to nearly 70 per cent. On the other hand, toxemia which occurs late in pregnancy in only a few cases in which the response to the test was always normal.

C. E. FOLSOME.

Smith, George Van S., and Smith, O. Watkins: Late Pregnancy Toxemia, West. J. Surg. 55: 288, 1947.

The late toxemias of pregnancy are the result of escape from the uterus into the general circulation of a toxic protein, resulting from tissue breakdown in the endometrium, as a result of premature withdrawal of estrogen and progesterone. The normal conversion of estradiol to estrone and estriol is facilitated by progesterone. Premature labor, intrauterine death, pre-eclampsia and eclampsia are associated with a premature drop in progesterone, which results in an incomplete conversion of estradiol, which is followed by tissue catabolism and

a release of toxin. The premature aging of the toxemic placenta collaborates and is a part of the events described above. The toxin liberated from the endometrium after premature estrogen and progesterone withdrawal is similar to the menstrual toxin resulting from tissue break-down in the normal menstrual cycle. The elevation of chorionic gonadotropin results from the failure of the aging syncytium to perform its normal function of utilizing it in the production of estrogen and progesterone. It is concluded that late toxemias of pregnancy are the result of a tissue toxin which results from tissue necrosis in the decidua following premature withdrawal of estrogen and progesterone. WILLIAM BICKERS.

Brouse, L. T.: Hemorrhage Following Toxemia, Obst. y Ginec. Latino-Am. 4: 749-762, 1946.

The author maintains that in the presence of toxemia, with its associated edema, the uterine musculature undergoes changes which result in dissociation of the fibers. The uterus therefore becomes atonic, and there is inertia during labor. During the third stage the inertia may result in hemorrhage, with consequent severe anemia and even death. At the El Salvador Maternity the mortality from the inertia and hemorrhage which result from toxemia was 10.1 per cent. The author believes that the association of toxemia and uterine inertia with hemorrhage is much more frequent than is generally admitted. There is no relationship between the severity of the toxemia and the degree of atony of the uterus or amount of bleeding. The author favors expectant and conservative therapy for toxemia chiefly in the form of sedation, blood transfusion and medical induction of labor by the method of Kreis.

J. P. GREENHILL.

Venereal Disease

Becker, S. William: Practical Aspects of Verification Tests for Syphilis in Office Practice, Am. J. Syph. Gonor. & Ven. Dis. **31**: 225, 1947.

The author concludes that on the basis of a small series of cases, the Kahn verification procedures seem to support the multiple diagnostic attack of Stokes in evaluation of positive blood tests as seen in private syphilologic practice. They are not recommended for the nonsyphilologist.

The use of cardiolipin and purified lecithin (Pangborn) and use of newer chemical methods devised by Neurath promise to be of even greater assistance in identification of nonspecific positive blood tests. C. O. MALAND.

Callaway, J. Lamar: The Weltmann Serum Coagulation Reaction in Syphilis, Am. J. Syph. Gonor. & Ven. Dis. **31**: 216, 1947.

The author summarizes the article as follows: (1) The results of the Weltmann serum coagulation reaction in 610 patients with syphilis are given. (2) With the exception of thirty-four patients with prenatal syphilis, the Weltmann coagulation reaction band was either normal or revealed a tendency toward moderate but distinct shift to the right with a prolongation of the coagulation band. (3) Thirty-two patients with early syphilis received six months' treatment with an arsenical and bismuth, without appreciable change in the Weltmann coagulation band. (4) Fever therapy and penicillin therapy in patients with syphilis of the central nervous system exerted no specific effect on the Weltmann coagulation reaction band. (5) Sex or race seemed to exert no effect on the Weltmann reaction band in this study.

C. O. MALAND.

Correspondence

Pulmonary Embolism From Amniotic Fluid

To the Editor:

In the December, 1947, issue of the JOURNAL, Drs. Leo Seltzer and William Schuman[1] reported a possible case of nonfatal pulmonary embolism by amniotic fluid contents. The authors described a syndrome of cyanosis, dyspnea, tachycardia, shock, and pulmonary edema occurring during delivery under general anesthesia. X-rays revealed bilateral areas of increased density without atelectasis or mediastinal shift. These areas cleared approximately ninety-six hours later. The authors also considered the possibility of aspiration of gastric contents but discounted this because of the absence of any recognizable anesthetic difficulties and the absence of atelectasis in the roentgen findings.

The aspiration of gastric contents during obstetric anesthesia can produce two entirely different syndromes.[2] There may be gastric retention of solid or liquid material during labor. The aspiration of solid food usually produces laryngeal or bronchial obstruction. Complete obstruction produces suffocation. Incomplete obstruction produces massive atelectasis with the classical picture of cyanosis, tachycardia, shock, dyspnea, mediastinal shift, and signs of consolidation over the collapsed area. X-rays reveal a homogeneous density and varying degrees of mediastinal shift. The pathology and treatment of atelectasis are well recognized.

The aspiration of liquid material produces a syndrome with distinct clinical, roentgenologic, pathologic, and therapeutic features. This syndrome had apparently escaped previous recognition. There is cyanosis, tachycardia, dyspnea, and shock, but no massive atelectasis or mediastinal shift. Wheezes, râles, and rhonchi are heard over the affected portions of the lungs. X-rays reveal irregular, soft, mottled densities without mediastinal shift. The picture has been confused with pulmonary embolism, bronchopneumonia, tuberculosis, fungus infection, and even metastasis. Progressive cardiac failure and pulmonary edema may supervene, regardless of the previously normal condition of the heart. Here the diagnosis has been confused with primary heart failure. Experimental work indicated that gastric hydrochloric acid produces a bronchiolar spasm and a peribronchiolar congestive and exudative reaction interfering with normal intrapulmonary circulation. Therapy should be directed against the bronchiolar spasm and cardiac embarrassment. Oxygen, atropine, adrenaline, and aminophylline will accomplish these objectives. Rapid intravenous digitalization is indicated in the event of cardiac decompensation. Bloodless tourniquet phlebotomy will further relieve the circulatory burden. Stellate ganglion block was also suggested. The bronchoscope would appear to be of little value for the pathologic process is beyond reach, and endoscopy may only increase the existent spasm and dangers of secondary infection. The majority of patients have an afebrile recovery with complete clearing of the chest in seven to ten days. The pathologic process is primarily irritative and not infectious but prophylactic use of chemotherapy or antibiotics may be of value. This type of aspiration may be prevented by withholding all oral feeding during labor and substituting parenteral routes where necessary. Alkalinization of, and emptying the stomach contents prior to the administration of a general anesthetic was also suggested among other prophylactic measures.

The case reported by Drs. Seltzer and Schuman also suggests that their patient could have aspirated liquid gastric contents. The clinical, roentgenologic, and therapeutic features support this diagnosis. It is not surprising that the actual aspiration could have gone unrecognized, for in the study[2] referred to, it was undetected in 32 per cent of cases. I have questioned the diagnosis of embolism of amniotic fluid contents to draw attention to the

liquid aspiration syndrome, since the latter probably occurs more frequently and is preventable. Although the authors have not been didactic about their diagnosis, they have apparently overlooked another explanation for their findings.

References

1. Seltzer, L. M., and Schuman, W.: Am. J. Obst. & Gynec. 54: 1038, 1947.
2. Mendelson, C. L.: Am. J. Obst. & Gynec. 52: 191, 1946.

Curtis L. Mendelson, M.D.

New York, N. Y.
January 18, 1948.

Reply by Drs. Seltzer and Schuman

To the Editor:

In reply to the letter by Dr. Mendelson concerning his comments on the diagnosis of the case reported by us,[1] we wish to state at the outset that the diagnosis of aspiration of stomach contents was not "overlooked," as stated by Dr. Mendelson. In our discussion of "Differential Diagnosis" under item No. 4, "Aspiration of Blood or Stomach Contents," we specifically discussed that possibility. In deference to Dr. Mendelson's fine contribution to our knowledge of the pathologic physiology of the effects of aspiration of stomach contents, of which we were aware at the time we wrote our article, we could not omit the possibility of that syndrome.

There is no question that the clinical syndrome described by Dr. Mendelson[2] *AND* Drs. Steiner and Lushbaugh[3, 4] have great similarity. However, from the point of view of mode of onset, there is great disparity. Dr. Mendelson's original paper describes an "Asthmatic-Like Syndrome" which he ascribes to the irritative effect on the bronchial tree of aspirated hydrochloric acid in the stomach contents. One would assume that this would produce a severe cough following restoration of reflexes after the obtunding effect of a general anesthesia has worn off. One patient did not cough until *11 hours* following the cessation of anesthesia (productive of frothy, pink sputum) and coughing is not mentioned in a single fatal case reported by Steiner and Lushbaugh,[3, 4] Hemmings,[5] and Gross and Benz.[6] It is our impression that clinically coughing would constitute a very important differential diagnostic criterion. In pulmonary embolization, the severe shock (which our patient demonstrated initially) is most striking, with cough developing subsequently, as the effect of the pathology produced by the embolism increases.

Further evidence to enforce our diagnosis are the following facts of our case:

1. The patient ate her last full meal the evening before admission (fourteen hours).
2. She had only a cup of coffee for breakfast one hour before she was admitted, not in labor.
3. No solid food was given during her labor and only a bowl (approximately 200 c.c.) of broth was given per os during her labor of 11 hours and 12 minutes.
4. There was no evidence of vomiting throughout her labor and she was rather closely observed by the house-staff physicians and nurses during this period because of "breech" presentation.
5. There was no coughing, retching, or vomiting during the induction of the anesthesia and none during or following the delivery. Aspiration produced no fluid or particulate food when the patient went into the profound state of shock described.
6. According to the statement of the anesthetist (one of the full-time anesthesia staff) the induction was very smooth and the amount of anesthesia required was minimal. This has been verified several times.

In spite of the well-known fact of delayed emptying time of the stomach during labor, it hardly seems likely that our patient had sufficient solid particulate food in her stomach, that might have been aspirated, to produce the syndrome we described. Dr. Mendelson points out very significantly that, in 32 per cent of the cases at the New York Hospital,

aspiration of stomach contents was unrecognized, and this may also be true in our case. However in view of the history and findings this possibility seems remote.

Finally, and we become repetitious, aspiration of stomach contents would not give the roentgenologic evidence of bilateral pulmonary infarction which our patient presented.

As this discussion indicates, as yet an absolute diagnosis of pulmonary amniotic fluid content embolism cannot be made in the living patient. Gross and Benz[6] suggest an excellent blood sediment technique worked out on postmortem cases, in which three definite layers of material, the uppermost being particulate amniotic fluid material, appear in cases of pulmonary embolism by amniotic fluid. However, as they state, the blood must come from the right side of the heart or inferior vena cava, which limits its clinical feasibility prior to demise.

In closing, we wish to thank Dr. Mendelson for his interest in our paper, and the editor for the opportunity of answering Dr. Mendelson in this column.

References

1. Seltzer, Leo M., and Schuman, William: Am. J. Obst. & Gynec. **54**: 1038, 1947.
2. Mendelson, Curtis L.: Am. J. Obst. & Gynec. **52**: 191, 1946.
3. Steiner, P. E., and Lushbaugh, C. C.: J. A. M. A. **117**: 1245-1254 and 1340-1345, 1941.
4 Lushbaugh, C. C., and Steiner, P. E.: Am. J. Obst. & Gynec. **43**: 833, 1942.
5. Hemmings, Clarence T.: Am. J. Obst. & Gynec. **53**: 303, 1947.
6. Gross, Paul, and Benz, Edward J.: Surg., Gynec. & Obst. **85**: 315, 1947.

Leo M. Seltzer, M.D.
William Schuman, M.D.

Baltimore, Maryland.
February 7, 1948.

Cornification in the Cervix and Estrogenic Activity

To the Editor:

Recently an interesting study by Ayre (Ayre, J. E.: Am. J. Obst. & Gynec. **54**: 363-389, 1947) has appeared. In it, he hypothecates an ingenious theory of the possible causation of cervical carcinoma, stressing three factors: chronic inflammation, dietary deficiency, and estrogenic activity. It is concerning the last of these factors that some discussion seems in order.

Ayre states, "The vaginal cornification count provides a simple method of obtaining a reasonably accurate estimation of endogenous tissue estrogens . . ." Later he observes, "the cervical cornification counts were found to be almost consistently higher than the vaginal cornification counts in the same cases." Thus, in 87 per cent of 125 cases studied "without regard to disease," he noted higher cornification in the cervical than in the vaginal smear.

Cornification in the smear is not always the result of estrogen stimulation. Papanicolaou has noted it frequently in chronic inflammatory processes of the cervix or the vagina. Intercourse may produce it; it is increased in cases of threatened abortion. Infection with the *Trichomonas vaginalis* often produces a very high cornification—at times even after the cessation of menstruation.

In many instances of cervical malignancy, there is an associated cervicitis due to secondary infection, and a surprising number of these women have a trichomonas infestation. It may therefore be argued that the cornification in such cases is due to the infection rather than to the carcinoma.

Greene and Peckham (Greene, R. R., and Peckham, B. M.: Am. J. Obst. & Gynec. **54**: 611-616, 1947) also question the validity of using the vaginal smear alone as a quantitative index of endogenous estrogen production. They point out that cornified smears may be found in postmenopausal women.

Finally, if one takes a cervical smear by scraping the surface, he will obtain a correspondingly higher per cent of cornified cells, since these cells are located in the more superficial layers of the stratified squamous epithelium. Conversely, the vaginal fluid serves to dilute the concentration of cells, and these cells represent a desquamation from all layers of the vaginal and cervical mucous membranes. It appears obvious that cervical smears taken by scraping will usually contain more cornified cells than vaginal smears taken with a pipette.

These considerations do not detract from the interest which Ayre's contribution should arouse. It is merely felt that his contention that cornification is an index of endogenous estrogenic activity may possibly be modified by some of the factors mentioned.

LOCKE L. MACKENZIE, M.D.

471 PARK AVENUE
NEW YORK CITY.
Jan. 21, 1948.

Reply by Dr. Ayre

To the Editor:

Dr. Mackenzie's interesting remarks provoke further discussion relating to cornification and estrogenic activity.

He states, "Cornification in the smear is not always the result of estrogen stimulation. Papanicolaou has noted it frequently in chronic inflammatory processes of the cervix or the vagina. Intercourse may produce it; it is increased in cases of threatened abortion. Infestation with the *Trichomonas vaginalis* often produces a very high cornification—at times even after the cessation of menstruation." We, too, have observed increased cornification in smears in chronic inflammatory processes. The question arises: Does this argue against the proposed theory of concentration of estrogen in inflamed or in irritated tissues or does it strengthen the concept? It would seem logical that the "repair hormone" might be concentrated as a defense mechanism at the point of injury or damage.

There are many things that we do not know about cornification and estrogen metabolism. In intercourse, may you not have an increased exfoliation of surface cornified cells to account for the apparent rise in cornification? In cases of threatened abortion we, too, have observed the rise in cornification. Is this not due to a fall in the antagonistic luteal hormone rather than a quantitative increase in estrogen?

It is perhaps important to differentiate, too, between pseudocornification, which is an acidophilic-staining cell with a large immature nucleus, and true cornification, which is the mature end product of pure growth stimulation, a morphologic interpretation of a cell with a small, mature, cornified nucleus. The nuclear morphology is of greater significance than the acidophilia.

In our experience, the acute or subacute stage of inflammation is associated with some increase in true cornification, but a greater proportion of acidophilic cells which are pseudocornified. This is the picture we have found in patients with primary trichomonas infestation, e.g., even in virgins without signs of other disease. Our contention has been that the chronic inflammation has been perhaps the primary factor focalizing the area of proliferation. Then the concentration of the cornification in this region of proliferation has been secondary to the inflammatory state. While we cannot be dogmatic as to which was first in the cervix, the inflammation or the cancer, a certain amount of our evidence suggests that the inflammation preceded the malignant change.

The evidence for the concentrations of estrogen found in the cervix is the finding of cornified cells concentrated in the normal squamous epithelium encircling the squamo-columnar junction. Therefore, in the preclinical cancer, in the cervix which looks normal, yet harbors an early cancer, the same scraping with the spatula which reveals the unexpected cancer cells scrapes also the adjacent normal-appearing squamous epithelium. In this epithelium is found the concentration of cornified cells. On the other hand, in the presence of a large ulcerating

clinical cancer, obviously, smears or scrapings from the cervical opening would yield only cancer cells, blood, and secretion. It would be necessary to scrape the squamous epithelium adjacent to the growth to obtain the cornification index in this tissue.

While the vaginal smear, or better, the selective scraping method, as a quantitative index of endogenous estrogen, is far from ideal, what better method do we have available today? The cell method seems to be superior to proliferative activity as measured by endometrial biopsies. The fact that cornified smears may be found in a small number of postmenopausal cases does not indicate that this is a normal finding. May it not be that this small group of women who show this, do possess some disorder of estrogen metabolism which may possibly endanger them to some of the influences which may ultimately produce a carcinoma?

We are in agreement with Doctor Mackenzie's arguments regarding the method of obtaining smears. The vaginal fluid, undoubtedly, serves to dilute the concentration of cells. However, when a vaginal aspiration was compared to a cervical external os aspiration in early cancers (in which the squamous epithelium of the junction remained close to the cervical os), the higher concentration of cornified cells was usually found in the cervical smear. Comparative scrapings in the same patients from the cervix and from the vaginal wall confirmed the higher concentration of cornified cells in the cervical epithelium. Obviously, smears must be compared only to smears, and scrapings to similar scrapings from a different area.

J. Ernest Ayre, M.D.

Montreal, Quebec.
Feb. 14, 1948.

Endometriosis and Estrogen Therapy

To the Editor:

Endometriosis and adenomyosis are now being reported by careful gynecologic surgeons and pathologists in one out of five pelves. Many of those reported are symptomless, but fairly regularly the diagnosis is made and conservative surgery used as therapeusis. Numbers of these patients then are seen by other medical men, who do not understand, or fail to take cognizance of, the implications of the diagnosis of endometriosis. These patients are subsequently placed on estrogen therapy. This therapy in turn can be in the form of minimal doses which seem not to stimulate the endometriosis very much, but I have seen numerous patients who have had large doses of estrogen and who have had marked reactivation of their endometrial symptoms.

I should suggest that, whenever a diagnosis of endometriosis is proved, either at the operating table or in the pathologic laboratory, the patient be instructed that she is never to have estrogenic therapy for any reason whatsoever, unless full cognizance is taken of the possibility of recurrence of the remaining endometriosis and the possible results of such therapy.

Lowell F. Bushnell, M.D.

Los Angeles, Calif.
March 10, 1948.

Necrology

FREDERICK W. RICE, M.D., obstetrician and gynecologist of New York City, died there on March 30, 1948, at the age of 68. He was a graduate of the College of Physicians and Surgeons in 1906, and served as surgeon with the rank of Captain in the first World War. He was an attending obstetrician at Bellevue Hospital, Professor of Obstetrics at the New York University College of Medicine until his retirement in 1934, consulting obstetrician in several hospitals, Fellow of the New York Obstetrical Society and the American College of Surgeons, a Diplomate of the American Board, and active as a Roman Catholic layman in the New York Archdiocese.

Item

American Board of Obstetrics and Gynecology, Inc.

The general oral and pathology examinations (Part II) for all candidates will be conducted at Washington, D. C., by the entire Board from Sunday, May 16, through Saturday, May 22, 1948. The Shoreham Hotel in Washington will be the headquarters for the Board. Formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates. Hotel reservations may be made by writing direct to the Shoreham.

Candidates for re-examination in Part II must make written application to the Secretary's office not later than April 1, 1948.

Candidates in military or naval service are requested to keep the Secretary's office informed of any change in address.

Applications are now being received for the 1949 examinations. For further information and application blanks, address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh 6, Pa.

PAUL TITUS, M.D.